THE NATURAL HISTORY OF DISEASE

Oxford University Press, Amen House, London E.C. 4

GLASGOW NEW YORK TORONTO MELBOURNE WELLINGTON

BOMBAY CALCUTTA MADRAS CAPE TOWN

Geoffrey Cumberlege, Publisher to the University

OXFORD MEDICAL PUBLICATIONS

THE NATURAL HISTORY OF DISEASE

BY

JOHN A. RYLE

M.A., M.D., F.R.C.P.

Professor of Social Medicine in the University of Oxford
Consulting Physician to Guy's Hospital, London, and the Radcliffe Infirmary, Oxford
Formerly Regius Professor of Physic in the University of Cambridge

SECOND EDITION

GEOFFREY CUMBERLEGE
OXFORD UNIVERSITY PRESS
LONDON NEW YORK TORONTO

'In writing, therefore, a history of diseases, every philosophical hypothesis which hath prepossessed the writer in its favour, ought to be totally laid aside, and then the manifest and natural phenomena of diseases, however minute, must be noted with the utmost accuracy, imitating in this the great exactness of painters, who in their pictures copy the smallest spots or moles in the originals; for it is difficult to give a detail of the numerous errors that spring from hypothesis. . . .'

THOMAS SYDENHAM
(From *The Works of Thomas Sydenham, M.D.*)

'Symptoms are universally available; they are the voice of nature; signs, by which I mean more artificial and refined methods of scrutiny—the stethoscope, the microscope, &c.—are not always within the power of every man, and with all their help, are additions, not substitutes.'

JOHN BROWN
(From the Introduction to *Horae Subsecivae*)

'Every pain has its distinct and pregnant signification, if we will but carefully search for it.'

JOHN HILTON
(*Lectures on 'Rest and Pain'*)

Second Edition 1948
Second Impression 1949

PRINTED IN GREAT BRITAIN AT THE UNIVERSITY PRESS, OXFORD
BY CHARLES BATEY, PRINTER TO THE UNIVERSITY

TO

A. F. H.

IN FRIENDSHIP AND
GRATITUDE
FOR MUCH
INSPIRATION

PREFACE TO THE SECOND EDITION

A LITTLE over a decade has passed since this book was published. It has, I gather, had quite a number of friends. Although the original issue was by then exhausted, the publication of a second impression during the war was rendered impossible by reason of the paper shortage. The publishers have now kindly asked for a new edition.

It has been instructive to peruse again these records of earlier experience and the reflections based upon them. Apart from a measure of discontent with the style and arrangement of certain passages I find myself approving, on the whole, the descriptive and critical portions of the book. The clinical portraiture of certain diseases and their course, which it was my main object to provide, together with the strong plea for a maintenance and reinforcement of the older disciplines of observational medicine, may well be allowed to stand. Main conclusions and recommendations call for no drastic revision. The 'physician as naturalist' remains a proper ideal, for no amount of scientific training or technical ability—and we live in a highly technical age—can supply those qualities of naturalist and of humanist without which the good physician can never fully earn his title.

Where, however, I have discussed the effects of therapeutic measures on the natural progression of certain infections, several chapters have fallen badly out of step. The arrival of the sulphonamides and penicillin has completely altered the course and prognosis of the streptococcal, staphylococcal, and pneumococcal fevers and has improved the treatment of infections with *Bacillus coli*. Earlier therapeutic opinions have therefore been revised in several places but, since treatment is considered chiefly in its relation to course, and since the new therapeutic techniques are still in process of development and my own experience of them is very limited, I have entered into no detail. I decided, however, to leave the chapter on pneumonia as it stood. It would be a pity if the student were to lose interest in

prognosis and in the difficult judgements which it requires, with some of which this chapter deals. Just as the twentieth-century student has diminishing opportunities of 'knowing' syphilis, so, too, will he come to lose his chances of 'knowing' the pneumococcal, meningococcal, and septic fevers, which he combats or aborts to-day with increasing confidence. The prognosis of pneumonia at all ages, and even in the elderly, has already been greatly changed. Even pneumococcal meningitis, with its mortality formerly never far from 100 per cent., has become a more curable complication with the aid of the new remedies. The long and painstaking trials of specific sera which were subjected to a critical review in Chapter XIX can now be relegated to the realm of past endeavour, but the types of judgement requisite for assessing new methods are the same. In the case of all these grave bacterial infections and of others which we may shortly learn to counter, I should like to enter a plea for better attempts in future to arrive at more reliable statistical assessments of mortality and morbidity. To make this possible much better standards of clinical recording will be necessary. Until 'cures' can be computed on a statistical basis we cannot form precise judgements on specific or supposedly specific remedies. Nor should we ever forget, for all our new skills, that Nature is still 'the physician of diseases'.

The sulphonamides and penicillin in many hands are being wisely used and often with appropriate methods of control. In many others they are being employed in haphazard fashion, almost as a panacea for unexplained fevers and for symptoms which have been but indifferently understood. Clinical medicine is brought into daily disrepute by such neglect of basic disciplines.

As a successor to Chapter XIX, I have included a new one dealing more generally with the uses of prognosis. Chapter XXXII, dealing with nosophobia—one of the most widespread of all diseases but often undiagnosed or too lightly regarded—is also new.

The natural history of disease in the individual is still the main preoccupation of this volume. The natural history of

disease in the community is a subject at least as worthy of attention. As a reminder of the importance of social studies of disease and of some of the methods and uses of what may best be described as *social pathology*, I have added a single chapter (Chapter XXXVI) bearing upon the natural history of rheumatic fever in this country. Social pathology has been curiously understressed—almost to the point of neglect—in the teaching of the text-books and the schools, but there are signs now of awakening interest and it can only be a matter of time before this branch of human pathological inquiry is accorded better status in our university departments. We cannot too often remind ourselves that, in the same period in which Addison, Bright, Gull, and Wilks were laying improved foundations to human medicine and the pathology of the individual, Chadwick and Farr were laying the foundations of our social medicine and pathology—the former by his great surveys and the close correlations of disease with poverty and squalor which he revealed; the latter by the new mathematical precision which he added to socio-medical investigation and the power which he imparted to the dead to speak on behalf of living and unborn generations. Outside the public health field, bedside pathology has continued to absorb the attention of most doctors to the exclusion of a parallel interest in the ultimate and contributory causes and social consequences of all the more prevalent diseases. But social and individual pathology are interdependent sciences and prevention is still more important than cure. In a more socially conscious era we are beginning to move forward again and the intimate study of health and sickness and their aetiologies—in families, schools, occupational groups, and larger populations—will shortly give a new impetus to academic and practical medicine. Most of our text-books need rewriting. Students are becoming avid for information and for types of experience which are rarely offered them in the hospital ward and the laboratory.

Numerous small corrections have been made to the text, but the general character of the original chapters remains unchanged.

I am indebted to the Editor of the *Journal of the Royal Sanitary Institute* for permission to incorporate as Chapter XXXVI (with some additions and minor modifications) the substance of an address given at the annual conference of the Institute at Blackpool in 1946; and to the Editor of the *Guy's Hospital Gazette* for the inclusion (as Chapter XX) of a modified version of an address to the Pupils' Physical Society given in 1938; and (as Chapter XXXII) an adaptation of a clinical lecture given in 1941.

J. A. R.

Oxford 1947

PREFACE TO THE FIRST EDITION

Of the thirty-four papers here collected the majority have appeared previously in the medical journals of the past ten years and are based upon addresses to medical societies or clinical lectures given at Guy's Hospital. Their concern is with subjects of general medical interest, and more particularly with symptomatology and the portraiture of disease. They are to be regarded as gleanings from the current experience of a general physican. Other occasional essays, bearing broadly upon the natural history of disease or the methods and ideals of its students, have been added.

In the biological sciences as a whole experiment and laboratory observation have by no means abolished the necessity for field work. Indeed the importance of field work is being more than ever widely acclaimed. With medical science it should not be otherwise and, although the journals of to-day are so largely occupied with the results of bio-chemical, bio-physical, and bacteriological research, there is still, I believe, ample scope and genuine need for plain clinical description and discussion. The physician is, in fact, and will remain the field-naturalist of those numerous branches of human biology which Medicine comprises.

With this for justification, my decision to republish these lectures and essays in book form is further due, in no small part, to the kindly comments which several of them have attracted from colleagues in this country and the United States and to the advice of friends. I am much indebted to the editors of the *Guy's Hospital Reports*, the *Lancet*, the *British Medical Journal*, the *Proceedings of the Royal Society of Medicine*, the *Practitioner*, the *Clinical Journal*, and the *Guy's Hospital Gazette* for their permission to include papers which have appeared in the columns of their journals. Dr. R. E. Smith, of Rugby, has kindly allowed me to include my portion of a paper on 'Streptococcal Fever' which we wrote in collaboration. To many friends in practice who have given me the opportunity of extending my experience

by sharing theirs, and to my old teachers and my fellow students at Guy's, I should also like to express my gratitude, for their inspiration and their criticism have often helped me to set my thoughts in order.

Modifications and corrections of the original text have been necessary here and there, and some case-histories have been added or substituted for better illustration of a theme. No naturalist, however careful, can pretend that his conclusions are free from error, but I can justly say, with William Heberden, that 'the notes, from which the following observations were collected, were taken in the chambers of the sick, from themselves or from their attendants, where several things might occasion the omission of some material circumstances', and that I have throughout been at pains to eliminate ill-judged hypothesis and to avoid undue reliance upon impressions and memories. Full notes, frequently perused, are the essence of clinical education. In the keeping of my case-notes I have been blessed with willing and expert secretarial aid, for which my thanks are due to Miss Nora McDonald. In the betterment both of original manuscript and proofs I have had the wise and patient assistance of my wife.

J. A. R.

London
January 1936

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I

THE PHYSICIAN AS NATURALIST[1]

In that part of his discourse on *The Advancement of Learning* which concerns the work of the physician, Bacon remarks, 'Only there is one thing still remaining, which is of more consequence than all the rest: namely, a true and active Natural Philosophy for the Science of Medicine to be built upon.' Ever since his day, with the genius and leadership of great minds like Harvey's and Hunter's, with discoveries due to experiment in the hands of men like Jenner and Lister, with steady accumulations of knowledge due to the observational schools of Heberden, of Bright and Addison, of Laennec and Trousseau, and the contributions of the physiologists and pathologists, our profession may be said to have been laying and proving those foundations. Should criticism of the work in our present industrious, if less illustrious, age be asked, it would, I think, be to the effect that in rearing the superstructure we incline too often to a neglect of that philosophy which has provided and must still provide the mortar as well as the foundations of all the sciences.

It is my plan, in reviewing some functions of the physician, to consider especially what part he has played and may continue to play in providing the bricks and mortar of 'a true and active Natural Philosophy' in medicine. An 'active philosophy' we may, presumably, take to mean a progressive one, having practical bearings, and in no sense 'abstract'.

Now the functions of the physician are manifold. There is probably no servant of the community of whom a greater degree of omniscience is demanded, or upon whom a graver responsibility in respect of personal and sometimes social guidance is, from time to time, imposed. As a rule, differing but little in native endowments and early training from others who are given the advantages of a higher education,

[1] An address given to the Cambridge University Medical Society, 29 April 1931 (*Guy's Hosp. Rep.*, 1931, lxxxi. 278).

he is nevertheless expected to combine in his person the attributes of scientist, healer, priest, and prophet. Furnished in general with no more grey matter than his brothers in other professions, he is yet believed by many of his patients, and even by some of the more intelligent among them, to have the key to secrets unknowable as well as known. It is almost as if they suspected him of some of the magic powers of the 'medicine man', to whom, in his guise of unqualified or qualified 'quack', they are only too ready to fly if orthodox endeavours fail to convince or cure them.

In point of fact, most physicians are no more than good, honest fellows seeking to do their best according to their lights, in an arduous profession and in the face of great difficulties, by a combination of humane feeling with careful observation and common sense superimposed upon a background of scientific education. Although the two may go hand in hand, the physician's material success is by no means always a measure of his ability. The former depends not a little upon personality, appearance, and powers of persuasion. The latter, as I shall hope to show, is a measure of his aptitude and training as an observer of nature. Skill in diagnosis and prognosis comes only with careful and continued schooling in observation; therapeutic achievement is seldom outstanding unless it be based upon accuracy in diagnosis, judgement in prognosis, and psychological insight, for all of which a proper understanding of the natural history of disease in man and of man in disease is a necessary equipment.

In taking 'the physician as naturalist' for my theme, I am therefore electing to discuss him in relation to what would seem to be his most essential function.

The Meaning of 'Physician'

Now the conception of the physician as a naturalist is at least as old as Hippocrates, the first among physicians and one of the greatest of the early natural philosophers. With the passage of time, however, the name has come to convey ideas of another kind. It is well that we should pause occa-

sionally to consider the *original* meaning of words in common use. In an address[1] given in 1888 Professor W. T. Gairdner of Glasgow (from whom, being unable to invent a better, I have borrowed my title, although my reflections on the subject are of a different sort), reminded his audience that the word *physician* must originally have implied not a healer, but a student of *φύσις* or nature, and that *physic*, which we now think of as meaning a drug or a medicine, must have had the same derivation. On the basis of this derivation he made it his opening argument that it should be the prerogative of the physician 'to be trained and exercised after the best manner and according to the most thorough discipline of the science of his age; and that he ought to be (or, at least, that he has been in very remote times) regarded as being admirable and trustworthy as a healer or physician, chiefly in proportion to the confidence reposed in him as a *naturalist*, that is, a humble, reverent and exact follower and student of Nature'.[2] To this argument, although specialization and other developments in our profession have come to vary the equipment and calling of its individual members, we should all subscribe.

In pursuit of my programme I shall seek to compare the spirit and functions of the naturalist with the spirit and functions of the physician; to consider how far the achievements of certain great physicians in the past have depended upon their ability as naturalists; to remind you of some among them who were recognized also as good natural historians in the usual sense of the term; and to insist that the training and ideals, now and in the future, for all that is truly physicianly in the work of the general practitioner, the consultant, and the specialist, are just the same training and ideals which are regarded as essential for the development of the good naturalist. With a brief digression on the contributions of observation and experiment, I shall conclude with some remarks on the selection and training of the physician and on the manner in which his difficult course may best be laid.

[1] *The Physician as Naturalist*, Glasgow, 1888.
[2] Op. cit.

The Spirit and Functions of the Naturalist

In the naturalist we behold, or so it seems to me, the cultivation and ultimate development of all that is commendable in the native inquisitiveness of childhood. The young of *Homo sapiens*, when wisely handled and neither curbed with rebukes nor frustrated with lies, commonly ask the most searching and sensible questions, and are ever seeking to know not only 'What?', but also 'How?' and 'Why?'. They are often acute observers, and it is in their desire to understand natural phenomena that we find them most avid and most interesting. But alas, when, in happier circumstances, we might guide him in his natural bent and foster an embryo Darwin, hoary custom and the educational systems of the country snatch our child away to have his head packed with instructions and book-lore until, in most instances, the desire to know by observation and experiment is crowded out and his feet are set in the fixed pathways of a routine or official life. He becomes a business or professional man. His relief from drudgery is found in sport, or sometimes in literature or art. He loses the inquiring faculty and ceases, as a rule, to ponder the entrancing problems of life and the great environment of life. Our admiration for those who keep and foster the inquiring faculty in spite of the toils of a stereotyped schooling should therefore be an exalted one. Our naturalists, retaining the clear-eyed curiosity of youth, both feed and reward it with the experience and wisdom of years. For ever seeking first-hand knowledge, they are for ever refreshed and in turn refresh all human thought.

Naturalists are of many kinds and creeds, but they hold certain attributes in common, and notably the desire to establish the truth of things by observing and recording, by classification and analysis. Some of them are in a sense specialists in that they confine their attentions to a single branch of natural study, and that, maybe, a small one. But the term 'naturalist' is employed as a rule in a wider sense, and the naturalistic temperament, I believe, forbids rigid specialism. Thus, you will commonly find that a man

widely known as a specialist in one branch of science has, actually, far wider interests. A friend of mine, chiefly eminent in the field of morbid histology, in his spare time earns an almost equal eminence for his knowledge of beetles and is no mean botanist, while those who meet him in friendly converse and read his papers know him for a student of philosophy.

Our country has been peculiarly rich in naturalists. Let us take three examples—men of widely varying heart and calibre, but all to be counted among the heroic figures of natural philosophy. Darwin in the immensity of his endeavour and the majesty of his thought towers above the rest. It is interesting, and in support of my contention, that his boyhood education was altogether a failure; he hated being taught and could not learn in the traditional way. Experience was his sole school. He observed, he collected, he recorded, and he deduced. His knowledge extended over fields immeasurably wide and applied itself to details infinitely small. He considered, it would almost seem, every form and attribute of living matter. Had medicine not been distasteful to him, and presumably too confined a subject and too set about with unpleasing interruptions to thought, he might have become the greatest physician that ever lived, for he would have left no stone unturned in his will to discover everything knowable about Man in health and disease, about Man in relation to his environment, his ancestry, and to his natural enemies in the shape of sickness and injury. No narrow specialism would ever have applied its blinkers to him. He would have embraced anatomy, physiology, pathology and psychology, anthropology and sociology in his grasp, dissecting, assessing, and moulding them and learning their proper places in that whole which we call Medicine. Such giants, we know, are rare and not to be emulated, but their inspiration is gigantic also and abides.

Huxley was another giant but of a different kind. He too had an amazing intellectual grasp and clarity of vision, and added to these a fine combativeness. We know him for zoologist, physiologist, and palaeontologist, very much

a naturalist and in no sense specialized. A great opponent of dogma and tradition in education, a staunch advocate for giving the natural sciences an ever more prominent place in our educational system, a fine exponent of his own knowledge and of that acquired by others, and possessed of a literary ability rare in scientists, he will remain for all time one of the great and progressive influences in naturalistic thought. What a fine Professor of Medicine he would have made! How he would have rent the old orthodoxies, and forced common sense, keen observation, and the importance of cultivating the critical faculty on his students.

And next let us take Gilbert White of Selbourne, that peaceful, parochial sage, watching his birds and his seasons, his flowers and his weather-signals; noting all down in his diaries with minute care as to time and dates; observing behaviour in wild things; experimenting with echo and dewponds; tilting at superstitions; and handing down to a grateful posterity his homely and truthful records. Most fitly did a friend, recognizing the wide influence his *Natural History* would have, write to congratulate its author with the remark that 'it will correct men's principles'. Faithful observation of matters of fact in nature must ever, in a world of ignorance and prejudice, serve to 'correct men's principles'. To do so indeed is a main function of the naturalist.

If Darwin might have been a greater Hippocrates and Huxley the greatest Professor in Medicine, Gilbert White would surely have supported all that is finest in the history of general practice, where so much sound learning about disease, about man in conflict with his environment, about man in all the stages of his individual growth, about the inborn and extraneous factors in disease, and about the practical handling of the sick, is garnered. Alas that so great a part of it should pass unsifted to the grave with its tired and tried discoverers.

We might select other types of naturalist for comparison —Linnaeus, Waterton, Yarrell, Buckland, Fabre, or, of more recent memory, Hudson, with his patience and strong sympathies and happy gifts of style. In each, I fancy, we

should discover qualities which have pertained to learned or kindly and practical physicians through the ages. The spirit of the naturalist is the spirit of science combined with that of philosophy; it seeks to 'correct men's principles'; to enlarge men's outlook; to pursue and teach truth for truth's sake; to increase and correlate knowledge; and to make what is remarkable or beautiful in nature more interesting, and what is interesting more beautiful or remarkable.

The individualist function of the naturalist is to satisfy his own intellect. His function in the community is partly, indeed, to educate and inspire, but the practical applications of his work in man's affairs are also to be regarded. Genetics, stock-breeding, forestry, agriculture, fisheries, public health, medicine, and psychology are in debt not only to the Darwins and the Huxleys, but to an army of humbler disciples in general zoology, botany, entomology, or other branches of natural knowledge.

The Spirit and Functions of the Physician

If we exclude for the moment (although they too were essentially naturalists) the great discoverers in physiology like Harvey and the great discoverers in the realm of public health like Jenner, both of whom on a basis of close observation evolved an historical experiment, we find that the ranks of the famous physicians are chiefly filled with men belonging to the observational school. These made no such great revolution in thought or practice as did Harvey and Jenner, but they provided by degrees the chapters of a great uncompiled 'Compendium of the Natural History of Disease'. Of such were Hippocrates, Sydenham, Laennec, Trousseau, Heberden, Bright, Addison, Gull, Wilks, and Osler. Hippocrates left us the first detailed case-records, studied symptoms and the influence of seasons, and wrote a book of remarkable aphorisms and a system of prognostics. Now prognosis clearly depends upon a knowledge of the natural course or history of disease and of the manner in which this is influenced by age and sex and season and treatment; prognostic ability is a special mark of the good physician.

In an age in which quacks and charlatans abounded—not that they nre not plentiful to-day—be insisted on an understanding of the nature of man and his diseases as an essential preliminary to any therapeutie system. Of his observational ability we have repeated records in *Epidemics* and in the *Aphorisms*, wherein he describes the frothing urine of nephritis and the 'eurved nails' whieh develop in empyema; and records the had prognostie significance of hiccup in kidney disease, of spasm (tetanus) following wounds, of speechlessness and stertor in apoplexy, and of the association of n large, hard liver with jaundice, and so fortb. His experience must have been immense, his powers of observation most aeute. He was surely a very great naturalist.

Sydenham, by his deseriptions of fevers and gout, and other maladies, faithfully followed the Hippocratic system. Pursuing his plan of 'improving pbysic' hy 'eollecting a genuine and natural description or history of all diseases as can be procured' he earned for himself the title of 'the English Hippocrates'.

Heberden, with a clear style and eommendable brevity, described tbe diseases which he encountered in his practiee and left us the first and the ahlest description of angiaa pectoris. His method he explains in the prefaee to his *Commentaries on the History and Cure of Diseases* in the following words:

> 'The notes, from which the following observations were collected, were taken in the chambers of the sick, from themselves or from their attendants, where several things might occasion the omission of some material circumstances. These notes were read over every month, and such facts as tended to throw any light upon the history of a distemper, or the effects of a remedy, were entered nnder the title of the distemper in another book, from which were extracted all the particulars here given, relating to the nature and cure of diseases.'

You will remark how careful he is to dispense with the serviees of that fickle handmaid, memory. All good physicians and naturalists eadeavour to take their notes at the time of their observations, in order to possess true records for comparison and analysis, and to secure accuracy in anything which they may subsequently write.

Bright and Addison, the two great physician-pathologists of the Guy's school, combined with the most careful study of disease in man an equally careful examination of the body after death. On the basis of their case-records they were able to establish the identity of the diseases which have been named after them, and of many other conditions since clearly recognized, but before their time unfamiliar because their thorough observational methods had not come into vogue.

If we read the lives and writings of these great physicians we cannot but be impressed by their industry and their eager spirit of inquiry, which, often with sacrifice of time and health, became the central motive of their lives, the constant claims upon their professional services notwithstanding. The spirit which actuated them was the same spirit which actuated the great naturalists. Their function was identical. It was to improve knowledge, to 'correct men's principles'. If in the process it often happened that the principles of treatment as well as the general recognition of disease in man were furthered, their social utility was only the more enhanced.

Now you may object that I have chosen for my comparisons only the more eminent among the naturalists and the physicians. That is true. I have done so because we of the rank and file have drawn so much inspiration from them and because it is good to remember indebtedness. At the same time, however, and in the same way, if in a lesser degree, it is certain that all other naturalists or physicians worthy of the name have subserved and will continue to subserve these functions, moved by the same spirit to render their contributions to human knowledge.

Physicians who were also Naturalists

If the spirit and functions of the naturalist and the physician be so similar it would not be surprising to discover that physicians have commonly been naturalists in other fields. This is indeed the case. Many of us are no doubt acquainted with family doctors who are experts in ornithology, entomology, or botany or in some other branch

of natural science. If you should have the chance to peruse the earlier volumes of the *Philosophical Transactions* of the Royal Society you will be interested to note how frequently contributions on widely various scientific subjects came from the hands of medical men. If you examine to-day the membership lists of any big society such as the British Ornithologists' Union or of any local natural history society you will find, I think, that the medical profession is better represented than any other. Although I have no such records before me, I can assemble at once to my mind a long list of able naturalists among my colleagues in general and consulting practice. There are also notable examples of men who set out to become doctors but were soon more powerfully attracted to other fields in natural philosophy. Darwin, Huxley, and Buckland were among these.

All this but serves to show that the naturalistic temperament and the physicianly temperament are, as we should imagine, close relations, if not identical twins. It also lends support to my contention that the physicianly or naturalistic temperament is expansive and out of accord with specialism. Although other examples might be quoted, I am content to refer to two great physicians only who were no mean naturalists outside their professional lives. Edward Jenner, the discoverer of vaccination and, incidentally, the first to associate angina pectoris with disease of the coronary arteries, published a very important paper on the cuckoo in the *Philosophical Transactions* for 1788. He also anticipated Darwin in some observations on the utility of earthworms, and was very helpful in furthering experiments and securing specimens for John Hunter, who had a great regard for him. In one of his letters to Jenner, Hunter, then engaged upon experiments on hibernating animals, writes: 'I own I was glad when I heard you was married to a woman of fortune; but "let her go, never mind her". I shall employ you with hedgehogs, for I do not know how far I may trust mine.'

Richard Bright, before he settled down to his historic work at Guy's, had accompanied an expedition to Iceland,

acting as zoologist to the party, and later contributing notes on botany and zoology to Mackenzie's *Travels in Iceland*. At the age of twenty-nine he produced a remarkable quarto volume of *Travels from Venice through Lower Hungary*, in which he sets out, with the same meticulous care and the same precision in observation which we see later in his medical writings, all that he could note of places and people, of customs and dialects and the general conditions of life abroad in the course of a long and none too comfortable journey. It is interesting to compare his *Travels* and a volume of his beautifully documented and illustrated *Reports on Medical Cases*.

The Natural History of Disease in Man

It might be supposed that the natural history of disease in man would be a main concern of the modern physician just as it was a main concern of Hippocrates and his earlier disciples. I am doubtful whether this supposition could be universally supported to-day. *Tempora mutantur*, and with them the scope and method of physicians. It becomes necessary to remind ourselves how rapid advances in learning may sometimes serve to make the principles and conduct of a science or profession more rather than less difficult. Discoveries in physiology, biochemistry, and bacteriology and the constant introduction of new methods of clinical inquiry have so far added to the burden of the medical curriculum and complicated the training and the work of the medical man that it has become, for the time being, increasingly hard for him to hold the scales of judgement and to maintain what Gull called 'the general view'. By the demands of examining bodies the student spends roughly two-thirds of his time with the preliminary and ancillary sciences and one-third only with patients. He embarks upon this latter third of his course with his thoughts rightly imbued with the importance of experiment and of laboratory methods, but is asked of a sudden to contemplate the bewildering problem of man in disease. Even in the wards he is often encouraged to think too biochemically or radiologically, for many of the cases there are problematical and

admitted for special investigations, and he does not see enough of disease in its simpler forms and early stages and in its natural environments. With some accidental bias acquired at this time he may very readily come to think overmuch in terms of chemistry or bacteriology or surgery. It is at first wellnigh impossible for him to win through to that point of vantage from which medicine can be regarded as the general 'biology of man in disease', and not as a congeries of loosely linked sciences and specialisms concerned with parts rather than wholes, and often rather with the 'seed' than with the 'soil', which is, actually, his more immediate concern. At no point, as a rule, is he offered the strong helping hand of a broad medical philosophy. No wonder he is sometimes confused or even disappointed, and frequently attracted into a service, a laboratory, or a specialism, wherein, as it seems, he can apply himself contentedly to a limited field of facts, or acquire a technical skill which will bring him bread and butter and a sufficiency of interest. How is he to acquire the 'general view', how shall he learn to become more of a naturalist and less of a receptacle for laboratory lore or the tenets and teachings of individual professors?

I cannot but feel that of late, in the process of pursuing the small and special truths which relate to the causes and more intimate processes of disease, we have as a profession been falling into the error of neglecting the large and central truths which concern the nature of disease itself. It is clear that the word *disease* holds very different definitions for different people. For the patient it *is*, in a literal sense, *his* dis-ease, his pain or breathlessness, his distress of body or mind. For the pathologist, the surgeon, or the physician it holds other interpretations. Let us take an example. A duodenal ulcer to the pathologist is a small punched-out, circular lesion situated just distally to the pyloric sphincter, having a smooth edge and in the process of its development destroying one or more coats of the intestinal wall. Around it he visualizes with his microscopic eye a thickened submucous layer with varying stages of fibrosis. To the surgeon as therapeutist a duodenal ulcer is apt to appear as

a small local evil to be excised or circumvented with skilful handicraft and recorded as another 'conquest', with the happy sequel of a patient sent on his way rejoicing—unless he be among those unfortunates who suffer a relapse. The physician as naturalist can take no such restricted view as either of these. He thinks of 'duodenal ulcer' in terms of a peculiar and interesting type of hunger-pain of rhythmical periodicity, associated with the local condition which the pathologist describes, afflicting persons of particular physical and psychological types, occurring five times as frequently in men as in women, showing a definite familial tendency and a pronounced seasonal fluctuation, and carrying with it liabilities in respect of haemorrhage, perforation, scarring, or intermittent disability from a wearisome dyspepsia. He is aware that it has at first a natural tendency to self-healing and that in its earlier stages such healing can, under suitable conditions of dietary and physiological rest, be encouraged and consummated for long periods or even through life. In later stages the tendency to relapse in spite of treatment increases. As a physiologist he appreciates its common association with a native hyperchlorhydria and the high, short stomach which the radiologist reveals. His studies incline him to the view that focal infections and nicotine, but perhaps still more the mental and physical fret and stress of civilized city-life, contribute to the perpetuation, if not to the actual causation, of the disease. He knows that without knowledge of this kind his treatment and prognosis in individual cases, and his decision as between a medical or a combined surgical and medical campaign of treatment, would be ill judged and insecure. He endeavours to study the disease from every possible angle, as an ornithologist might study the morphology, the habits, and the environment of a bird. By information so gathered, information which the particular teaching of pathology, biochemistry, surgery, or radiology, whether severally or in concert, could never give, he gradually establishes his claim to an understanding of duodenal ulcer in man, and of man afflicted with duodenal ulcer, as reasonable and complete as present conditions will allow.

Or take some wholly different malndy like pneumonia. The laboratory-man may think of it in terms of 'antibodies' and varying types of pneumococcus, and if he dabbles in therapeutics may hold himself justified in prescribing treatment with vaccine or serum. The physician knows that nt certain ages and in certain patients the disease will run n particular course to spontaneous recovery within n certain brief time, and that in such case it would be wholly unwise to experiment with medicines, vaccines, or sera. In children after the first year or two lobar pneumonia is pnrticularly benign. In adult life there is a much less certain outlook, and there is a mortality which varies with season, with country, and with epidemic, all factors which make it extremely difficult to form judgements about the efficacy of remedies. Certain conditions, such as alcoholism, greatly raise the mortality of pneumonia. In individual enses there are symptoms and signs which compel a hopeful, n guarded, or a pessimistic outlook. Knowledge of this kind, with its intimnte benring on the conduct of cases, can only come through prolonged study of the disease in man. Animal studies and bacteriology mny be helpful, but they are often misleading.

It now becomes pertinent to return to our question in regard to the nature and definition of a disease. Clenrly it is not merely a symptom or a group of symptoms; it is not the local injury nor the general poisoning which gives rise to the symptoms; nor yet the bacterial invasion which gives rise to the injury (or the poisoning) which causes the symptoms. Might we not define a disease as '*the whole consequence of a conflict between man (or animal) and the noxious agencies in his environment*'? This includes the concept of 'soil' as well as 'seed', and indeed of all the intrinsic and extrinsic factors at work. Sydenham said, 'A disense, in my opinion, how prejudicial soever its causes may be to the body, is *no more than a vigorous effort of nature* to throw off the morbific matter, and thus recover the patient.' It is, in other words, just as much a natural phenomenon as health or as man himself, its victim, are natural phenomena, and as such it should be studied.

Pneumonia or any other disease in an individual may be influenced in its course, not only by the type of the invading microbe, but also by the age and type of the patient, by his hereditary endowments, by his environment and his psychology, and even, as Hippocrates knew, by the psychology of his attendants. Unless we can appreciate all this we are not good naturalists and we are not in a position to diagnose (or 'thoroughly know'), to 'prognose' (or forecast), and to treat as ably as we might do. A knowledge of the natural history of disease is essential in therapeutics. Gull and Sutton[1] studied the natural history of rheumatic fever by treating a series of cases with mint-water, and were thereby able to show that certain remedies then advocated had no appreciable influence on its course or behaviour. From time to time 'cures' for problematical diseases like disseminated sclerosis are announced by physicians who have not been at pains to familiarize themselves with the long remissions and psychological reactions peculiar to the malady.

Diseases, like races, vary in character at different times and in different places. They may, like races, under varying conditions, appear and disappear, as we have witnessed in the case of chlorosis. These features in their history are also worthy of attention.

The Natural History of Man in Disease

Perhaps I have already made the study of disease appear too vast and difficult for you by insisting on the value of what Smuts[2] would call the holistic view (from ὅλος = whole). In point of fact, and given a reasonable interest in one's fellow men, this is really a simpler doctrine than that which is commonly offered to the medical student in the later clinical period of his training. Here he is confronted, at what should be the summit and summary of his pre-graduate education, with a loosely connected series of

[1] *A Collection of the Published Writings of Sir William Gull*, New Sydenham Society, 1894.

[2] *Holism and Evolution*, by General the Rt. Hon. J. C. Smuts, Macmillan, London, 1927.

special studies, which have lost touch with physiology, which separate part from part, and cause from effect, and give him, as a rule, but little clue as to what are essentials and what non-essentials in human medicine; which find their material altogether too much among the 'end-result' diseases of the hospital ward; and which have for their aim not so much a reasoned understanding of common problems as the satisfaction of individual teachers and the passing of examinations.

I have postulated a 'reasonable interest in one's fellow men' as necessary for the holistic or naturalistic view of disease, for the proper study of mankind, whether sick or well, is surely man. He is the instrument whereby we study his diseases and, unless we know the varying temper of the glass, the delicacy of the gauges, and the mechanisms under the set experiments of health, we shall not rightly follow the processes of those experiments of Nature's which we call disease. Laboratory physiology can only tell us a tithe of the health-experiment. We have need of a broader and more observational human physiology, more cognisant of human variety. Every man is endowed at birth by his parents and ancestors with a type of constitution built of anatomical, physiological, immunological, and psychological material which will help to determine his course through life and his reactions to environmental stress or injury. With the aid of family histories and observations of physical and mental types we may learn to recognize or predict certain liabilities in the way of disease. Gout, asthma, pernicious anaemia, migraine, epilepsy, and tuberculosis all depend in some degree upon such constitutional variations, which are quite comparable with other biological variations, and, like them, transmissible, and which in medicine are sometimes called diatheses. But apart from these special and broader variations we quickly learn that every individual reacts a little differently from every other individual to adverse as well as to beneficent physical and psychic stimuli, or, in the old phrase, that 'one man's meat is another man's poison'. For this reason the physician must ever be developing his understanding of human types and

reactions. Until he attains a certain proficiency in this he meets with many pitfalls and handicaps. His task is not easy, and yet you shall prove for yourselves how the manifold things to be observed (whether on the large scale or minutiae) and how constant practice in the method continually maintain the fascination of his work, in the conduct of which he can scarcely fail to experience the same zest and the same rewards which the naturalist in other fields experiences. Eye and ear and hand and sense of smell must be trained to gauge the physical divergencies from the normal and the wide variations within the 'normal'. So, too, the mind may learn to watch and gauge the effects of psychology on disease and of disease on psychology. The assessments can rarely be quantitative, as in the case of your physical and chemical tests, and yet experience and a grouping of rough assessments between them will often lead to a high degree of accuracy in the final opinion. In chronic renal disease, for instance, a very close estimate of the degree to which the blood-urea has been raised may sometimes be accomplished by experience and bedside methods alone, and prognosis can be determined, as a rule, as accurately by these as by any combination of chemical tests. People sometimes talk of the physician's 'intuition' or 'clinical sense'. There is no such thing, unless we mean by the terms quick perception, quick memory, and quick piecing together and application to a present problem of past experiences. All the senses are the physician's weapons, but a good visual memory and a lively sympathy are his best allies. Like the modern naturalist, he must, metaphorically speaking, be ready to use his camera and his 'bide' as well as his eyes and his note-book. The embarrassed patient, like the wild bird, cannot be successfully studied if he is self-conscious or afraid.

Observation and Experiment

Discussion in the journals has lately centred around the question of the relative importance to medical science of observation and experiment. Certain sciences, such as chemistry, physics, and modern physiology, are essentially

experimental. Others, like zoology and astronomy, are observational. In the biological sciences as a whole it would seem that we can dispense with neither method, but that experiment in the future is likely to play a much larger part than heretofore. In psychology, for instance, which has been so largely an observational study, the experiments of Pavlov on conditioned reflexes have come to modify and stimulate ideas. Clinical science is essentially observational, and the present scope of human experiment is, for obvious reasons, small. Nevertheless, Sir Thomas Lewis[1] believes that future progress in medicine must largely depend on the application of experimental methods to man in disease. With his contention that there is room for whole-time and adequately remunerated research appointments in clinical medicine to further this project I am in full agreement. It is well, however, to remember that nearly all experiments have developed on the basis of earlier, painstaking observations of natural phenomena, and that there is actually no great dividing gulf between the two methods. As Huxley put it, experiment is only 'artificial observation'. The 'observer' uses the slow, vast, and difficult experiments of nature. The 'experimenter' creates his own conditions and is thereby able in a shorter space of time and with greater precision to obtain the necessary proofs for the establishment, to his satisfaction, of laws and principles in operation in nature. It is generally allowed that many of the most useful discoveries in science have come through experiment. Harvey's discovery of the circulation, Jenner's vaccination, and, more recently, Banting's discovery of insulin are noteworthy examples. Darwin and Hunter relied far more upon extended observation, but all of these, in point of fact, were at one time and another both observers and experimenters.

Briefly there can be no dispute about the merits of the two methods; they are complementary. Experiment is the offspring and pupil of observation and may in time achieve more than its parent, but in biology, and in the biology of man in particular, it can never supersede or become independent of its parent.

[1] *Brit. Med. Journ.*, 15 March 1930.

Those of you who are attracted to experimental science, as I sincerely hope some will be, would do well to remember that observational science provides a good training-school, and that without it, in medicine, the ideas upon which most useful experiments are based would not be born at all. You are quite rightly training yourselves and being trained now in the more exact methods of physiology. Shortly you will be asked to acquire the observational outlook in the wards of a London Hospital. You will naturally try to apply there the knowledge and principles which you have acquired here, and at first it may seem difficult, for the problems are varied and complex. When, however, with a growing capacity for observation, you begin to correlate bedside findings and the everyday symptoms of disease with physiological and pathological knowledge, then indeed medicine will become for you an earnest adventure and a delight to the mind. Then too you may claim that the holistic or naturalistic philosophy is beginning to display its harmonizing influence.

Most of you are destined for practice, and observation will be your chief standby, but it would be a poor thing if you had not also been given an experimental training and the understanding of deeper and more intimate processes based thereon. Some of you will go back to the life of experimental research, but you will go the richer for having seen the problems which Nature sets us, and I would urge you not to be in too great a hurry to return to the microscope or the test-tube and to forget the fuller, if often more baffling, life of the clinic, the out-patient department, and the post-mortem room.

The Selection and Training of the Physician

In placing before you the claims of general medicine I may at times seem to have spoken in a disparaging way of specialism, but I would not for a moment have you suppose that I regard specialism or specialists as unnecessary. Far from it. The field of knowledge is altogether too vast to be explored without the constant aid of more and better specialism. In medicine both laboratory and clinical specialism have made far-reaching contributions, and this particu-

larly in the last few decades. In practice we are in constant debt to specialist colleagues for the help and instruction which they give us. But, without a doubt, there can be too much specialism, and over-specialism, and a neglect of co-ordination and of what Bacon called 'universality', and Smuts would call 'wholes'; and this neglect, I believe, obtains at present, not only in our own profession but in the scientific world at large.[1] And, in common with many others, I must also maintain that there is real danger in specializing too young, before the intellect is proved and fit, and that we may and do behold around us already a breed arising which lacks much of what was admirable in the old physicians who were their own specialists, and much that is admirable in the abler specialists who are their own physicians. Among a group of honoured teachers I have been particularly grateful to two—the first a surgeon, and incidentally a Doctor of Medicine, with as keen an interest in the medical and pathological aspects of his surgical cases as any physician or pathologist could boast; the second a physician, a Fellow of both the Royal Colleges, who constantly taught by example the importance of 'the general view' and of close care and thoroughness in the routine examination of cases. And surely it is proper that every specialist, whether medical or surgical, should retain qualities appropriate to the naturalist or physician. You may, it is evident, require devoted application and long practice to become an able cardiologist or aural surgeon, but in neither case can you afford to confine yourself too closely to 'the part' or to neglect that 'whole' which includes both

[1] Bacon (*Advancement of Learning*) has a very concise commentary on 'specialism' and 'holism'. 'Another error . . . is the over early and peremptory reduction of knowledge into arts and methods; from which time commonly sciences receive small or no augmentation. But as young men, when they knit and shape perfectly, do seldom grow to a further stature; *so knowledge, while it is in aphorisms and observations, it is in growth;* but when it once is comprehended in exact methods, it may perchance be further polished and illustrate and accommodated for use and practice; but it increaseth no more in bulk and substance.'

'Another error, which doth succeed that which we last mentioned, is that after the distribution of particular arts and sciences, men have abandoned universality, or *philosophia prima*; which cannot but cease and stop all progression.'

your patient and the wider fields of human and medical experience. Conversely, the general physician and the general practitioner can never afford to neglect the contributions of specialism. They should never presume, and, indeed, they are generally far too humble to presume, the possession of a medical omniscience.

Some minds clearly prefer to seek a more perfect efficiency in a smaller field. The physician as naturalist prefers the broader study of man in disease, and in the process is ever grateful for the additional knowledge which comes to him through the specialist. There is a facetious definition which states that the specialist is 'one who knows more and more about less and less', and the dilettante 'one who knows less and less about more and more'. I would suggest that it is the proper endeavour of physicians and naturalists to know 'more and more about more and more'. Is the ambition too presumptuous? I believe not, if the task is entered upon with method and humility. Not all minds are suited to the task; and no more are all minds suited to a life of experimental research or clinical specialism.

It is just here, it seems to me, that those who have the privilege for a period to be your teachers might sometimes do more to help you in the selection of your careers, by dint of knowing your earlier inclinations and, when possible, more of your individual characters and tastes, being less persuaded than is commonly the case by the claims of their own departments. Informed as to your 'diatheses', they should be the better able to prognosticate. The man of action, ingenuity, and manual dexterity has generally shown signs of these attributes in early youth; he might well be advised (if he will but remember to be something of a physician too) to think of surgery or a surgical specialism. The devotee of the microscope or the laboratory bench will probably be happier in pathology, bacteriology, or biochemistry and, even if his father wants him to join him in the practice, should consider the alternative life. But if it were told me of another that he had from boyhood been interested in birds and beasts, or fossils or flowers; that he kept notebooks of his observations or made careful collections of

specimens; and that he was thoughtfully and widely informed in natural lore—then I should strongly advise him (if able to resist the call of country practice) to think of the physician's life as his destiny. I should know that he would never 'apply the blinkers', that his naturalist's sense would serve him in good stead, that he would continue to observe, record, and analyse the phenomena encountered at the bedside and in the consulting-room, and that he would in all probability make his own useful contributions to the study of disease.

And what of his training? In hospital, and later with his necessary examinations behind him, he should seek contact with patients whenever and wherever he can, given only that he has the sense to avoid ill health and mental weariness through excess of routine. He should attend and perform as many post-mortem examinations as possible. He may have to wait some time for practice, but when it comes he will find that he learns more from his private patients on the whole, if he keeps a card-index and good notes, than form his hospital cases. His case-books or files will be his 'cabinets', his good diagnoses (I employ the term in its fullest sense) his 'naturalist's finds'. At frequent intervals by re-reading and analysing his notes, after the manner suggested by Heberden, and sometimes by the writing of papers he should seek to discover how far his first-hand knowledge of disease has advanced. *There is no disease of which a fuller or additional description does not remain to be written: there is no symptom as yet adequately explored.* He should meet colleagues in all branches of the profession as much as may be, and picking what is likely to prove profitable among them, should attend the discussions of medical societies. If finance and opportunity permit he should also visit foreign clinics, but rather as a refreshment and with a view to seeing others at work and learning new methods than as an alternative to self-instruction. In addition to the practice of ear and eye and hand the practice of reason and judgement must be assiduously cultivated. We must, I fear, confess that sound logic is an all too rare display in medical writings and discussions. He should endeavour to

preserve a just balance in his assessments as between the physical and the psychological, and the constitutional and the environmental factors in the causation of his patients' maladies. He should read current medical literature critically and the old masters with reverence. He should not deny himself that 'leisure' which Hippocrates regarded as one of the essentials in the life of the physician, although he may find it hard indeed to win. A general interest in the progress of biology will keep him stimulated and alert. At times he will be weary and overworked, at times very worried; it is not likely that any excess of material benefits will come his way; but his life will be happy, for he will keep faith with his intellect and his calling and contribute his mite towards the foundation of 'a true and active Natural Philosophy' in medicine.

II

THE TRAINING AND USE OF THE SENSES IN CLINICAL WORK[1]

ONE summer afternoon I was conversing with an old Guy's friend in his garden on the subject of plant-scents, a subject to which he has devoted much study and some pleasant writing. Incidentally I was put through my olfactory paces among his herbs and acquitted myself rather favourably. Our talk then drifted to the use of the sense of smell in medicine, and, when I had quoted a little of my experience, he urged me to attempt a review of the subject. This I shall not do here and now, but my nose has on many occasions been so helpful to me in conjunction with eye and ear and hand that his urging did at least prompt me to the delivery of this lecture, in the course of which I shall have occasion to consider some of the distinctive odours of disease. For anything useful in my remarks you must thank him; for their deficiencies—and descriptions of sensory revelation are not easy—you must blame me.

Diagnostic success at the bedside may be held to depend firstly upon the historical analysis, and secondly upon our personal powers of observation, both of which are subject to the continual leaven of experience. Nothing is so variable as observational ability. Some have it well developed from childhood, men of the naturalist type. Some never acquire any facility for it, and repeatedly miss the obvious. The majority cultivate their aptitudes by degrees and adopt a middle level. Most of us improve with time and practice, but many take but little pains to refine and to register experience, and, for this reason, retard their progress in the *clinical arts*.

All the five senses are employed in observational medicine. Taste, it is true, we rarely call to our aid now, for Fehling and Benedict have relieved us of the necessity of tasting the urine in cases of diabetes. The eyes, the hands,

[1] *Guy's Hosp. Gazette*, 1933, xlvii. 421.

the ears, and the nose, in that order, remain indispensable, and much can be added to their usefulness by training and by a working knowledge of the fields of perception open to them.

I shall throughout confine my attention to the training and use of the unaided senses. Just as over-refinement or an excess of education may blunt the natural faculties of the child, so, I believe, a multiplication of the instrumental aids at his disposal may serve to blunt the primary faculties of the physician. I shall consider in turn sight, touch, hearing, and smell, mentioning some of their opportunities in clinical work and some of the ways in which the acuity and efficiency of each may be improved.

Sight

Setting aside the information gleaned from others we may say that diagnosis begins the moment our patient comes within view. Before we have addressed a word to him or her we are, or should be, taking mental notes of age, physique, stature, complexion, expression, temperament, and, in some cases, of peculiarities, deformities, or the patent and sometimes specific surface evidences of disease. There is a very genuine study in what may be called *the physiognomy of disease*. Laycock[1] long ago gave particular attention to it. Among the more striking and specific physiognomies we include the mitral facies, with its malar hyperaemia and dark crimson lips, its varying tints of purple, and, when failure is advanced and the liver engorged, its underlying icterus. The drawn, pale, anxious, grey-lipped Hippocratic facies of peritonitis, with 'sharp nose and hollow eyes', is fortunately much rarer than it was, thanks to the surgeons. And so is the risus sardonicus of tetanus. The broad, thick-lipped, impassive face of myxoedema, with the cheeks tinted 'a delicate rose-purple', as Gull described it, a slight underlying waxiness, a smoothness of the skin, and the receding hair-margin and scanty eyebrows, is very characteristic, but I have known it, when inspection was too superficial, mistaken for that of mitral disease, nephritis, or pernicious

[1] T. Laycock, 'Physiognomical Diagnosis', *Med. Times and Gazette*, 1862, i. 102.

anaemia. The anxious face of hyperthyroidism, with prominent eyes and bulging neck, presents no difficulties in the well-developed case, but I have often had cases referred to me in which the cause of a tachycardia or a breathlessness, a nervousness, or a loss of weight had passed undetected because slight and early eye-signs or the fine tremor of the extended fingers had not been observed.

The lemon tint of pernicious anaemia, not always to be readily distinguished from the more sallow tint of gastric malignancy, a disease which it may simulate in many other ways, is none the less characteristic. In gastric cancer it is more likely that there will be evidence of loss of weight, with the so-called cachectic appearance, and a slightly bluish nose is a frequent feature. The brick-red facies of polycythaemia, sometimes simulating rude health at a first glance, but often with a tinge of blueness or purple to modify opinion, is quickly confirmed by turning down the deep-red eyelid just as we do in looking for the conjunctival pallor of anaemia. The watery eye, the blotchy face, and the reddish venous nose of alcoholism, sometimes with tremulous lips and tongue, may give the clue to a correct interpretation of digestive or nervous symptoms. Acne rosacea may likewise prompt a diagnosis of gastritis. The slightly drooping lids and wrinkled forehead of tabes, and the Parkinsonian mask of paralysis agitans or past encephalitis, with its flat, unwinking, sad, uncomfortable lack of expression (quite different from the puffy impassivity of myxoedema), are strongly diagnostic. The dark greenish-brown of chronic obstructive jaundice, and the dirty muddy-brown pallor of uraemia, whether due to chronic interstitial nephritis in a young man or to prostatic obstruction in an old, are other examples of diagnostic colour-change.

In acute disease there are countless small accessory phenomena for the eye to observe, such as the labial herpes and active alae nasi of pneumonia; the rose-spots of typhoid fever, and, in grave cases, the involuntary twitching of the hand on the coverlet; the Stocker's sign[1] of meningeal irrita-

[1] James Stocker, an early apothecary to Guy's Hospital (1831–78), was an astute observer and drew attention to certain symptoms of irritability

tion, best shown in tuberculous meningitis; the petechiae of blood diseases or infective endocarditis. Nor should we forget the clubbed fingers of chronic lung disease, empyema, and infective endocarditis, and the transverse grooves on the nails which date a recent illness as described by Wilks.

But what I would like to emphasize is that all these visual signs have their grades or degrees just as the diseases which they portray have their stages, and it is the early changes we should be more anxious to observe and which training and experience alone can help us to recognize. It is surely a much better accomplishment to 'spot' a 60 or 70 per cent. haemoglobin with 'the naked eye' than a 20 per cent. haemoglobin; or an early hyperthyroidism than a 'typical Graves'. Book teaching is too apt to impress us with the appearances of developed or advanced disease. And, apart from those relating to structural or pigmentary modifications, there are the far more difficult, but no less valuable, assessments relating to character, mood, and temper. Until, for instance, we learn to read the varying grades of anxiety or the attempts to mask anxiety and to detect the hidden cancer-phobia in the features or behaviour of our patients, our efforts at psychological diagnosis and handling are only partially rewarded.

Let us now leave the *physiognomy of disease* and consider other morbid aspects, and especially *decubitus* and *gaits*, both of which come within the visual quarter of our observational field. The way the patient lies in bed and the way he walks may tell us little or much. You are all familiar with the orthopnoea and dyspnoea of cardiac and respiratory disease. It would take too long to digress here into the many observable varieties of dyspnoea which eye and ear may study conjointly. The fixed rigidity of meningitis is easy enough to recognize in the advanced case. Its early recognition in a case of obscure fever and headache or in subarachnoid haemorrhage may require the co-operation of

which distinguished the victim of meningitis from the more apathetic 'fever' patient. If, in a doubtful case, on attempting to raise the shirt to look for an eruption the patient assisted you, it was a case of fever; if he resisted it was one of head disease.

the hands, but the decision to make the further test is often prompted by the appearance of unwillingness in the patient to move his head from the pillow. The adoption of the knee-elbow position by a rheumatic child may be the first sign of pericarditis. Gull once surprised an anxious mother by telling her that her daughter with typhoid fever would recover before he had entered the sick-room. He had seen her sitting up in bed as he passed the door.

I need not describe to you in detail here the stamping, broad-based action of tabes dorsalis; the steppage, drop-foot gait of peripheral neuritis; the dragging spastic gait of the paraplegic and the hemiplegic; the festinant trot of the paralysis agitans; or the stiffening shuffle of old age. Their enumeration, however, brings me to the question of how we may best train our eyes to do better as time goes by. I would first of all tell you simply to make a rule of having a good look at every patient as he walks into your presence or sits or stands or lies before you. To avoid embarrassment ask a question or two by all means, but study him well meanwhile. The art of medicine is largely the art of noticing. You need to cultivate constantly both the enthusiasm and the watchful patience of the field-naturalist if you wish to obtain the full value and interest which clinical work can bring. Secondly, I would advise you—and it was of this that the gaits reminded me—to cultivate the habit of 'street-diagnosis'. In my ward-clerk days I and some of my contemporaries used to compete in 'spotting' gaits coming over London Bridge, or facies sitting opposite us in the tube. It is quite a good game, better than crossword puzzles, and helps to pass the time as well as to train the wits. I often used to wonder where my social duty would lie if I saw a patient in the street with a chancre on the lip, knowing the condition to be dangerous alike to himself and others. At last I was faced with what looked like such a lesion in a burly fellow travelling in a tram. He had a swollen, oedematous lower lip with an ugly, hard-looking scab on it and, hoping to coax him to Out-Patients, I made some tender inquiries, only to find that he had acquired it at 'The Ring' a few days previously, and that it was merely the septic

sequel of a straight left. 'Spot diagnoses'—and please do not think that I am anxious for you ever to depend on visual diagnosis alone—are fallible, but our mistakes are salutary in themselves and can be turned to good account. In a walk from the Borough to the West End you are hardly likely to miss seeing a few pathological gaits or an example or two of the facies of anaemia, alcoholism, or malignant disease. You might even keep a note-book of your 'bags' and confirm your opinions by reference to the text-books at bedtime.

Touch

The sensitiveness of hands and finger-tips must be almost as variable as their character and shape. I believe we chiefly fail in palpation through lack of the art of 'fine adjustment', to borrow a term from the microscope. It is scarcely ever necessary or useful to examine forcibly or roughly. Gross abnormalities we are only likely to miss if we are hasty or careless. But again it is the slighter abnormalities that are most valuable to us and our patients, and these are only to be detected by the cultivation of a technique which is at once gentle and searching. The texture and qualities of the skin and the hair, whether we are looking for myxoedema or testing the lost lustre in the locks of an ailing child, are assayed by the fingers as well as the eyes. The slight oedema of the skin over an empyema or other deep suppuration is more worthy of discovery than the deep and obvious pitting of hydraemic nephritis, and only the trained and expectant thumb and forefinger can do it. The tiny anal fissure, so often the cause of misleading and widely distributed pain and quite commonly missed, can be appreciated as well by the forefinger as by the speculum; the 'feel' of the lesion reminds one of the roughness of the button-hole in the lapel of one's coat. In the abdomen minor degrees of rigidity or guarding can only be appreciated if we cultivate the gentle habit and the flat hand. The spleen, so useful in many diagnoses, and so often missed in its lesser degrees of enlargement, may escape our notice through employment of the finger-tips instead of the margin

You might suppose that the ear would not be of great nssistance in abdominal diagnosis, but I would remind you that it tells us of hiccups, a grave development in peritoaitis and renal disease; that the succussion splash is a most useful sign in pyloric stenosis; and that there are borborygmi which matter and borborygmi which do not. The commonest are the almost musical borborygmi of the nervous maid waiting at table. There is another curious type of rhythmical bubbling in the stomach, synchronous with the respirations, which occurs in nervous enteroptotic women who have acquired a faulty habit of abdominal breathing. These are gastric in origin. But there are also intestinal borborygmi of grave import in chronic obstruction, which synchronize with peristaltic movements, subterranean in quality and recurring at more or less regular intervals. Without putting the ear to the abdominal wall, they may be readily located in the bowel. Finally there are sounds which I would characterize as 'hollow tinklings', which may be heard in cases of paralytic distension of the gut, or again in chronic intestinal obstruction. The sense of hearing, like the sense of sight, can only be trained and put to better use by paying attention, and by deeming nothing so trivial as to be allowed to escape your notice.

Smell

Lastly we come back to the nose. In civilized man the olfactory sense has undoubtedly lost a good deal of its primitive acuity. The sense of smell is much more easily tired than the other senses. Unfortunately, too, it is extremely difficult to describe smells. Colours and shades or shapes may be defined and given names; sounds may be given attributes both of quantity and quality; smells can merely be likened to other smells; they may be given degrees of goodness and badness, but our descriptions are sadly lacking in precision. I shall consider diagnostic smells under four headings:

1. The smell of the patient as a whole, as noted in conditions in which we are unable to assign the aroma to any particular excretion or exhalation.

2. The smell of the breath.
3. The smell of the excreta.
4. The smell of pathological discharges.

In the old days when the wards of the general hospitals were largely filled with fever cases, it was not uncommon to find ward sisters of experience who could diagnose a fever from its smell. Typhoid, diphtheria, and measles have been reputed to be so recognizable. Mr. T. B. Layton has recently told us in the *Gazette* of a dresser who had a 'good nose' for diphtheria. During the First World War I thought that I became familiar with the typhoid smell, but perhaps through lack of concentrated experience I would not guarantee to 'spot' any of the other exanthemata with my nose. I have often thought that the sweat of the phthisical patient had a particular odour, but I cannot describe it. The sweat in rheumatic fever is said to have a sour quality. Of other specific smells, the skin disease Favus has the smell of mice.

The breath has many important smells. The unpleasant breath of pyorrhoea is by no means the least important, and its presence may help to clinch a decision to treat radically mouths in which the outward appearances alone are not at first sight too bad. I have recently seen two victims of general ill health, one with a secondary anaemia, in whom the typical pyorrhoea odour at once attracted my attention to what was probably the primary cause. The breath of an alveolar abscess and of some antral suppurations is distinctly more foul than that of pyorrhoea.

Halitosis from bowel and liver disturbances is entirely distinct in character from the odours accompanying suppuration in the mouth. It is stale and vaguely reminiscent of the smell of faeces or bowel-wind, although quite distinguishable from them. In cases of pulmonary abscess or gangrene the breath, as well as the sputum, may be as putrid as anything encountered in medicine.

Turning to more pleasant odours, we should, most of us, be familiar with the so-called acetone odour of the diabetic. I find that noses vary enormously in their ability to detect this. My own is rather acute. I have diagnosed diabetes from the foot of the bed, and I can detect the ketonaemic

breath in any febrile child. I have formed the habit of asking my ward clerks to smell the breaths of diabetic patients in the wards, and when the pleasant, faintly fruity odour is evident to me I commonly find that it is undetected by something like one-third to one-half of the firm. Apart from making the diagnosis of diabetes in the presence of glycosuria it may also quickly settle the cause of a coma, and so help to save a life.

The uraemic breath is another important one, but difficult to describe. It is only moderately unpleasant. It has somewhat fishy qualities; it is not exactly a urinous smell, and yet it is reminiscent of urine just as halitosis is somehow reminiscent of bowel contents. I have not yet determined how constantly and at what level of the rising tide of nitrogen-retention it becomes appreciable in the breath, but it has helped me to the diagnosis and prognosis of advanced renal disease and on several occasions to a recognition of prostatic uraemia in cases in which the bladder symptoms were not pronounced, the urine contained little or no albumin, and the general symptoms had previously passed unexplained.

The following case is of particular interest:

A man, aged 56, was referred to me by Dr. Berry, of Watford, for general malaise, vague discomfort in the liver region, loss of weight, cramps, and thirst. A complete physical overhaul failed to reveal any conclusive signs of disease, but I made the comment that his breath had the somewhat fishy odour of uraemia. His urine was chemically normal and showed no casts, and his blood-pressure was normal. He was referred to Dr. Hurst's Clinic. Here the only outstanding findings were a blood-urea of 103 mgm. per 100 c.c. (about three times normal) and a poor urea concentration. He was thought to have a slight prostatitis, but there was no considerable enlargement of the gland. On a low protein diet he quickly lost all his symptoms, and gained weight, and two and a half years later was able to perform his full work and to play thirty-six holes of golf each Saturday and Sunday. After two more years of good health this patient was seen in an acute illness due to a right-sided pyonephrosis, with pronounced uraemia, but again recovered.

In cases of pyloric stenosis and obstruction there are frequently eructations of sulphuretted hydrogen. A description of 'rotten eggs' by the patient or a relative has many times

helped me to suspect or confirm the diagnosis. In gastro-colic fistula 'bowel-wind' is eructated.

It is clearly, on occasion, of the first importance to detect alcohol and drugs such as paraldehyde in the breath.

I have mentioned the exceedingly putrescent foulness of the sputum in pulmonary abscess and gangrene. In bronchiectasis the sputum is usually less foul, and it may be merely heavy, mawkish, and musty. In pulmonary tuberculosis the odour is slight and almost sweetish.

The urine has the same pleasant fruitiness as the breath in untreated diabetes. In bacilluria it is characteristically unpleasant and 'fishy'. The damp, ammoniacal odour above the bed in urinary incontinence may give an early hint of the gravity of a case or in neurology of spinal cord involvement. Faecal unpleasantnesses are very numerous and variable, but in ulcerative colitis they are of a constant type and particularly objectionable. Fatty stools from pancreatic or mesenteric disease are rancid. The smell of a 'faecal fistula' discharge is distinctive and separable on the one hand from the ordinary smell of faeces and on the other from that of pus infected with bowel organisms. The surgeon draws useful conclusions from the relative sweetness or foulness of purulent discharges both in respect of their nature and the progress of the case. During the First World War wounds infected with the organisms of gas gangrene were characteristically malodorous.

It is a natural inclination to avoid dalliance over pathological odours, and yet it is clearly our duty to improve our acquaintance with them. I would advise you, therefore, to train your noses in respect of breaths, sputa, and urines in particular, and to remember that they may occasionally give you just as valuable information as the laboratory, and in much quicker time. The nose may also be trained in the street and garden to sift and analyse smells which are ordinarily passed by.

Our final opinion, of course, in any case is based upon a compounding of sense-data and an analysis by the mind of all the information we have collected by all the means at

our disposal. The more accurately, however, we observe with our special senses, the more judicial will our choice of other methods be and the more accurate the final opinion. Do not think that the few illustrations I have given you are intended to do more than indicate the range of possibilities open to your unassisted eyes, hands, ears, and nostrils. Your daily life in clinical medicine will furnish you with others in plenty, some which are old and familiar and others which you will reveal to yourselves. I am conscious of having omitted certain distinctive observations now inaccessible in the lumber-room of my memory. The fact that they are inaccessible only shows that I did not attend to them at the time or register them afterwards as carefully as I should. Nothing in medicine is so insignificant as to merit inattention.

III

THE CLINICAL STUDY OF PAIN

WITH SPECIAL REFERENCE TO THE PAINS OF VISCERAL DISEASE[1]

Of all the symptoms for which we are consulted pain, in one form or another, is the most frequent and frequently the most urgent. Properly assessed it stands pre-eminent among the sensory phenomena of disease as a guide to diagnosis. And yet it must be confessed that our understanding of its nature and mechanisms, and consequently of its full significance in practice, remains peculiarly limited. We are naturally dissatisfied with invisible and imponderable evidence, and it is therefore no matter for surprise that recent years have witnessed the introduction into medicine of a host of objective methods of studying disease, and that the study of subjective symptoms has suffered contemporary neglect. The opaque meal and enema; pyelography; cholecystography; the electro-cardiograph; methods of blood analysis; the various chemical tests for gastric, hepatic, pancreatic, and renal efficiency; bronchoscopy; lumbar puncture and its developments; and the exploratory operation—all these, following in the trail of the stethoscope and the ophthalmoscope and older routine methods of physical examination, bear witness to our zest for objective information. It is, however, chastening to remind ourselves that, notwithstanding all the help derived from a judicial employment of them, these methods too have their limitations, and none of them is infallible. They are often useful in proving or disproving the existence of established organic disease; in increasing the accuracy of a clinical opinion; and in serving to differentiate one form of organic disease from another. They have greatly helped in decisions for or against operative intervention. They have undoubtedly exerted an instructive and a corrective influence. In some degree—although, to my mind, by no means so much as

[1] *Brit. Med. Journ.*, 1928, i. 537.

they might have done—they have even enhanced our appreciation of subjective symptoms. But their contributions to the early diagnosis of organic disease and to the study of functional disorders are necessarily restricted, and it is clear that without the initial indication of certain symptoms they could never be rationally employed. Moreover, their aid can rarely be invoked in urgent problems or in the homes of the people. There is a very real danger that by over-reliance on them, by too great an anxiety to give our patients the benefit of modern investigations, and by a waning confidence in our own clinical ability, we may come to lose the astuteness and wisdom of our forebears.

In medical education the introduction of these methods has not been an unqualified blessing, and the training of ear and eye and hand and the development of the power of inductive reasoning have suffered much. Every year I see a number of mistakes made through inappropriate, unnecessary, or excessive investigation. Not infrequently I have myself fallen into error for similar reasons; and not infrequently I have extricated myself from error by a return to first principles, by taking the history of the case again, or by making a more careful analysis of the patient's sensations—Nature's earliest signals of morbidity. It will be readily agreed that many of the best diagnoses and judgements are achieved with the unaided senses backed by experience. It will also be agreed that no course of action can train these senses unless it includes experience patiently garnered at the bedside and in the consulting-room.

If I were asked how the next considerable advance is to be sought and won in the field of clinical medicine I should say (with grateful acknowledgements to the influence of Sir James Mackenzie) by the intimate study of the physiology of symptoms, and (once more acknowledging our debt to other great pioneers in this field—notably John Hilton and Sir Henry Head) I would submit that our first concern should be a more extended and intimate study of pain.

This brings me to a consideration of method. Now, research into subjective phenomena does not commend itself to the laboratory worker, and cannot easily be pursued in

the experimental animal. It is presumably for this reason that even the more recent text-books of physiology are extraordinarily reticent on the subject of all excepting the superficial pains, and that the scanty references which they make to visceral pain are often misleading. Thus they nearly all declare that visceral pain is very inaccurately located, and devote more discussion to the occasional sympathetic or somatic than to the far more frequent visceral sensations. Experiments on the healthy human subject, such as those conducted by Hurst and his collaborators in the course of their work on the sensibility of the alimentary canal, are of necessity limited, and no amount of ingenuity can quite reproduce the experiments in disturbed sensation with which Nature herself provides us in our own bodies or those of our patients. The study of pain must therefore continue to devolve mainly upon the clinicians.

I wish that time would permit me to refer to the method and the classical contributions of the pioneers whose names I have mentioned, and to the valuable communications of others, including Ross, Morley, and Cope in this country, and of Lennander, Rudolf Schmidt, and others abroad. For my present purpose let it suffice to recall that, whatever the individual trend of these investigators may have been—whether anatomical, physiological, surgical, or neurological—the basis of all their researches was clinical observation.

Partly because the immensity of the subject compels selective treatment, partly because visceral pains have especially interested me in my work as a general physician, and partly because they seem to me to have suffered neglect in comparison, for instance, with the pains of nervous disease, I have chosen to confine my attention in this paper to the subject of pain expressing visceral disease. My remarks will fall into three sections. In the first I shall endeavour to summarize the present state of our knowledge of the physiology of pains affecting the hollow organs. In the second I shall outline a simple system for the clinical analysis of such pains—a system which really embodies nothing new, and which is in large measure applicable to the study of other pains. In the third I shall consider, with examples,

the practical applications of pain analyses, for, after all, the chief interest to the practising part of our profession of all such studies is their bearing upon the advancement of diagnosis, prognosis, and treatment.

Visceral Pain

The insensitiveness to ordinary tactile, thermal, and chemical stimuli of the serous and mucous coats of the hollow viscera has been established in various ways. Partly on this account Sir James Mackenzie became protagonist for the view that there is no true visceral pain, but only pain projected to the somatic tissues supplied by the same segment of the cord as that which supplies the injured viscus. This view still finds a few supporters, but common experience and experiment have rendered it untenable for the majority of students. There is reason to believe that Mackenzie latterly modified his earlier view to that more generally upheld, for in 1922, in response to certain observations of my own, he wrote to me as follows: 'It is to answer this question that I have spent a long inquiry and have come to the conclusion that the only known stimulus that produces pain in the tissues which are supplied only by the autonomic nerves is the contraction of muscle.' I would prefer, for reasons which will become apparent, that we should state the matter a little differently by saying that 'visceral pain is commonly due to an abnormal increase in tension in the muscular element of the wall of the viscus', for a positive contraction is not the only cause of increased tension or of pain.[1]

This conception of the cause of visceral pain can be equally well adduced in explanation of pains as diverse in character and circumstance as those of labour, of gastric ulcer, and of renal colic. But there are other observations accessory to the main conclusion which may be made in regard to the pains of visceral disease. These I shall

[1] In cardiac pain ischaemia (or the associated chemical accompaniments of ischaemia) would appear to be the main factor, and it is possible that the ischaemia with demonstrable pallor which accompanies muscle spasm may be a more important immediate cause of pain than the shortening of the muscle-fibre.

summarize as concisely as possible, referring to them as 'laws' of visceral pain for brevity and convenience, and implying thereby 'present beliefs' rather than 'unalterable truths'.

'Laws' of Visceral Pain

(1) Visceral pain has its origin in and is due to an abnormal increase in tension of the muscular element of the wall of the viscus, this increase in tension resulting either (*a*) from contraction of the muscle, or (*b*) from its failure to relax in the face of increasing intravisceral pressure. (Examples: (*a*) tonic spasm of the colon, (*b*) bladder pain in the early stages of retention before the muscle-fibres have become overstretched.)

(2) Relieving factors in visceral pain, other than those which merely deaden consciousness, are invariably factors which reduce intravisceral pressure or encourage muscular relaxation. (Examples: the relief of pain from the sudden perforation of a diseased appendix; the passage of a calculus; the taking of food in duodenal ulcer.)

(3) As would be anticipated if the truth of (1) and (2) is conceded, the severity of mechanically induced pain is in inverse proportion to the normal distensibility of the viscus. (Thus the most severe pains are found in disease involving tubes of small calibre and small distensibility, such as the ureter, the bile ducts, and the arteries; the more bearable pains in disease involving organs of wide calibre and a wide range of physiological distensibility and postural adaptability, such as the stomach and urinary bladder.)

(4) Visceral pain when occurring alone or dissociable from attendant pains in the somatic tissues or other viscera can be accurately located by the patient, the localization corresponding, not with any segmental nerve distribution, but with the surface marking of the viscus. (Examples: the loin gesture of renal pain; the sternal gesture of cardiac pain; the accurate indication of the point of obstruction in oesophageal and some colonic strictures.)

(5) Visceral pain, having its origin in muscle, is related to the functional activity of the affected viscus. (Thus it is increased or relieved by food or fasting in gastric and duodenal ulcer, by effort or rest in cardiovascular disease, just as pain in skeletal muscle is aggravated by use and relieved by rest.)

(6) Referred somatic pain or soreness in visceral disease may accompany (*a*) severe visceral crises of mechanical origin, (*b*) inflammatory or ulcerative disease of the visceral wall, and more particularly if this involves the muscular coat. (Examples: (*a*) arm pain in angina and testicular pain in ureteric colic; (*b*) cutaneous soreness in appendicitis and chronic gastric ulcer.)

(7) Sustained somatic pain or soreness in visceral disease persisting apart from recent crises of visceral pain implies inflammatory disease

of the viscus in question. (Example: scapular angle pain and interscapular pain and soreness in chronic cholecystitis.)

(8) Conversely, absence of somatic pains and soreness is the rule in cases of visceral pain dependent on functional derangements or due to obstructive lesions in the more distensible viscera. (Examples: chronic colon spasm; pyloric or colonic growths.)

It need hardly be remarked that in actual practice we often encounter confusing effects which result from the extension of disease or multiple lesions or from the 'spread' of pain due to temperamental factors or long-continued psychological or physical ill health. Such a qualification need not, however, damage these main conclusions. It would be impossible to detail here the accumulated evidence on the basis of which it has seemed justifiable to formulate the foregoing 'laws'.

The referred sensory phenomena, requiring for their production special circumstances, such as intensity or prolongation through an inflammatory process of the appropriate stimulus, are infrequent in comparison with the *local* phenomena, and so are of less constant diagnostic value. It would therefore seem fitting to devote our attention more particularly to the primary visceral pains. It is chiefly with these that I shall concern myself in outlining the scheme for the analysis of a pain which follows.

The Analysis of a Pain

When a patient comes to us with a complaint of pain it is customary and natural to ask him where the pain is felt and what its character may be. Each of us, no doubt, has his individual *method of approach*. Often a few direct questions and a little patience will elicit replies so informative as to put us immediately on the track of an accurate opinion, but there remain a host of '*difficult pains*' in which our simple routine brings no reward, and we are left 'wondering', or are compelled to proceed to the physical examination, which may, in its turn, prove *exasperatingly negative*. Even the 'further investigations', when we can indulge in such luxuries or send the case to hospital, do not necessarily supply the answer to our problem. *It is just in these cases*

that we feel the need for some fuller method of inquiry. A little reflection will show that *there are no less than ten reasonable questions which may be propounded in any given case of visceral pain*, and, indeed, of most other kinds of pain. Each of these questions has some direct bearing on the qualities or circumstances of the symptom, and so renders our investigation less haphazard. It is true that the answers to these questions must be accorded very variable marks for merit. We cannot expect to obtain consecutive or intelligent co-operation from all our patients, but this is no reason for abandoning the attempt. For our failures to 'establish contact' or to assess the reliability of replies we must hold ourselves at least in part to blame, and, profiting by them, must aim at an improved technique.

Of these ten questions two have a bearing on quality and quantity, and may be answered under the headings of (1) *character* and (2) *severity*. Three have a bearing on spatial relationships, and are answerable under the headings of (3) *situation* (including depth from the surface), (4) *localization* (or extent of diffusion), and (5) *paths of reference*. Three have a bearing on temporal relationships, and are answerable under the headings of (6) *duration*, (7) *frequency*, and (8) *special times of occurrence*. Two have a bearing on determining causes, and are answerable under the headings of (9) *aggravating* and (10) *relieving factors*. Over and above these questions directly relating to the pain our interrogatory must also include *associated symptoms*. All of these questions are concerned with the spontaneous pain experienced by the patient. At a later stage we proceed to examine for elicited visceral pain (or 'tenderness') and elicited somatic pain (or 'soreness').

Practical Applications

Now let us consider the practical utility of an analysis of this kind. What can we learn of the *character* of a pain? It is common knowledge that certain descriptive adjectives crop up again and again in the language of our patients, and these must be accorded their full due. Thus the pain of ulcer is usually 'gnawing' or of a dull 'toothache' quality;

it is sustained while it lasts—that is to say, it is not markedly fluctuating and never intermittent. In an acute irritative gastritis the pain may be peristaltic and intermittent. The secondary gastric pain of gall-stone dyspepsia is commonly of a 'bursting' character. The pain of angina pectoris, sometimes so agonizing as to defy description, is often referred to as 'crushing', or 'vice-like'. The pains of biliary and renal colic, devastating in their ultimate throes, are nearly always continuous and crescendo, and in no true sense 'colicky'; they start with a dull ache which becomes progressively more intolerable. The pain of enteritis or small intestinal obstruction is truly 'colicky'—that is to say, rhythmically intermittent, sharp, and griping while in action, but quickly giving place to ease between the spasms. 'Burning' pains are rarely indicative of gross organic disease. The most familiar example is the homely heartburn, with its unpleasant, but never agonizing, sense of a retrosternal and almost 'chemical' heat, although such evidence as we have suggests that it is, in common with strangury and tenesmus, an accompaniment of spasm. *Diffuse* abdominal burning sensations are chiefly encountered in depressed or emotional patients.

The *severity* of a pain is notoriously hard to measure. It is always well to discover from our patient at an early stage whether 'pain' or 'discomfort' is the more appropriate description. True pain is more likely to mean organic disease. Pains which are comparable with or worse than those of labour or which have required a hypodermic injection we accept as genuinely severe. The effect of the pain on the performance of daily duties or mental work or equanimity or sleep allows some estimate of *its gravity*. Recourse to hot bottles, or bed, or analgesic drugs may help in our assessment, but in this part of our inquiry more than any other our own observational powers in regard to temperament or other factors likely to raise or lower the 'threshold' of the individual to pain must be called into play.

The *situation* and *localization* of a pain are best determined by observing the patient's gesture, and, best of all, when the opportunity can be found, or made, to see him in

its grip. The more defined and accurately localized the lesion responsible for a visceral pain the more accurate and defined, as a rule, is the gesture of the patient. There are many significant gestures. A famous proprietary pill has caught in its advertisements the typical gesture employed by the victims of a kidney stone. The pain of ulcer is commonly indicated with the tips of the fingers applied to mid-epigastrium; the pain of a functional dyspepsia with the flat of a roving hand. The point of arrest of a ureteric calculus may sometimes be shown with a single finger. In cases of chronic colon spasm I have seen the course of the colon accurately traced by patients wholly ignorant of anatomy. Among the best recognized *paths of reference* are those involving the left arm in angina pectoris, sometimes extending to the right arm, and in either case usually confined to the inner aspect and reaching the elbow, the wrist, or even the ring and little fingers, and sometimes also rising to the neck or jaw; the scapular or interscapular pain (*not* shoulder pain) of gall-bladder disease; and the testicular pain of ureteric colic. Superficial and more often deep skin soreness may be of very real assistance in the diagnosis of gastric and duodenal ulcer, of some forms of appendicitis, of cholecystitis, and diverticulitis. Referred pain down the front of the thighs may accompany salpingitis and tubal pregnancy. The details of the search for zones of soreness have received full discussion in the literature and need not be considered here. Care is sometimes necessary to avoid confusion of a fibrositic tenderness with a true sympathetic hyperalgesia.

The *duration* of a pain has a very special significance, and may frequently throw light on the particular perturbation of function which the pain itself less surely expresses. Thus the intermittent pains of intestinal colic, so clearly due to peristaltic over-activity, last a few seconds only. The pains of an anginal seizure (excluding the sustained agony of coronary occlusion) rarely last more than a few minutes, and are relieved by the immobility which they compel. The pains of gastric and duodenal ulcer last an hour or more, until the stomach is empty or replenished. Biliary

and renal crises may continue for an hour or hours, and often enough until the blessed relief of morphine has been won. In each instance we can nicely correlate the time character with the physiological event.

The *frequency* and *special times of occurrence* of a pain are also instructive. Epigastric pain which recurs daily and with some constant time relationship to meals is almost certainly of gastric origin. Epigastric pain arriving at rare intervals, 'out of the blue', and independently of eating or other physiological exercise, should raise a suspicion of gall-stones or tabetic crises. Epigastric pain, absent at times of rest but immediately induced by certain efforts, is almost undoubtedly due to cardiovascular disease. Of *special times of occurrence* it is also noteworthy that angina, in concert with other 'spasmodic complaints', as observed by Heberden, has a predilection for the early hours of the morning after the first sleep. The hunger pains of duodenal ulcer often wake their victims between the hours of midnight and 2 a.m., and gall-stone pains at a somewhat later hour.

Among *aggravating factors* (taking again the better-known types of pain) exertion, cold, annoyance, and particularly exertion after food, may all be provocative of anginal seizures. Jolting is apt to evoke pain in cases of biliary, renal, and vesical calculus, and in sufferers from chronic colon spasm, a disorder which is highly responsive also to the influence of cold, fatigue, worry, tobacco, and purgatives. Gentle thumping of the loin will more readily evoke the pain of calculous renal disease than simple deep palpation. Of *relieving factors* rest of body and mind and warmth are common to the majority of painful visceral disorders. Amyl nitrite has an almost specific effect in anginal pain, but not so in the status anginosus of coronary occlusion. Alkalis and belladonna (both probably by facilitating pyloric relaxation) have a well-known efficacy in gastric pain. Abdominal pressure, ill tolerated in inflammatory abdominal disease, may alleviate the pain of intestinal colic.

Now I would not for a moment have it supposed that an interrogatory such as I have outlined can be employed by every busy physician in every case of visceral pain with

which he is confronted; but I would suggest that some such method is not only appropriate but essential if we are to prosecute a careful inquiry into any single type of pain; and further, that it may be of decided value in practice in elucidating what I have described as 'difficult pains', and more particularly in those unhappily plentiful cases of chronic abdominal disease in which physical signs are scanty or altogether lacking. I can think of nothing better calculated to stay the epidemic of injudicious abdominal operations than an extension of interest in pain as a diagnostic symptom.

If I were asked to enunciate a few important principles for the everyday clinical study of pain my choice would fall upon the following:

First, in obscure cases and important decisions to try, whenever possible, to see the patient when his pain is present, for then, and then only, will his own observations be accurate and reliable, and not dependent upon memory, and physical signs, absent at other times, may be in evidence. We all know how few and far between (especially in consulting and hospital practice) are these opportunities of seeing our patients in pain. This circumstance alone is evidence of the rarity of continuous pain (excepting in advanced inflammatory and malignant disease), and supports the contention that visceral pains come and go in a physiological sequence and in obedience to physical laws.

Secondly, to pay particular attention to the patient's gesture, and, if he makes none spontaneously, to ask for a manual demonstration with the clothes removed. 'A pain in the stomach' may mean a pain anywhere between the manubrium sterni and the symphysis pubis, and our endeavour must ever be in the direction of greater accuracy. I have several times seen the mistake made of supposing a pain to be gastric because it was related to food. Colonic pains may also be influenced for better or worse by food, but they are situated in the lower abdomen, whereas gastric pains are always epigastric.

Thirdly, to remember the close association which exists between visceral pain and the functional activity of the

viscus in question. I once had a case referred to me by a cardiologist on a suspicion of stomach trouble with a request for a gastric analysis. The patient was an elderly man complaining of high epigastric pain after food. Before examining him I ascertained that the same pain was also evoked by walking, and that the case was undoubtedly one of angina pectoris.

It remains for me to cite from my personal store a few case histories which serve to show the value of a full analysis of pain, and how such an analysis may lead to a more correct opinion or may modify judgement or treatment in important ways. I have been careful to include mistakes of my own as well as those of others. How often these mistakes give us insight into matters previously debatable or obscure!

CASE 1. *A case in which examination of the patient during an attack of pain altered the diagnosis from duodenal ulcer to gall-stones.*

A surgeon consulted me in 1925 for symptoms which had troubled him at intervals since 1917. His main complaint was of epigastric pain, relieved by food and alkalis and occasionally waking him at 2 a.m. He always carried alkaline lozenges in his pocket. I found slight but definite tenderness and muscular guarding below the right ribs. A radiologist who examined him on two occasions reported some irregularity of the duodenal cap, but would not commit himself to a diagnosis of ulcer. A fractional test-meal showed a slight degree of hyperchlorhydria. I diagnosed duodenal ulcer. On the strength of a long history and frequent recent recurrences, I was inclined to advise operation, but it was finally agreed that he should lie up and undergo a strict medical treatment as for ulcer. A few days after starting the treatment he developed a severe epigastric ache which persisted for more than two hours in spite of alkalis and vomiting. Morphine was given for the relief of pain, which returned at 5 a.m. the next morning. At 8 a.m. I saw him again and was able to feel an enlarged gall-bladder. There was no pyrexia or icterus. A week later Mr. R. P. Rowlands removed a thickened gall-bladder with stones. The duodenum was healthy.

In referring to my original notes of his case I then found one significant entry which should have impressed me more. *In the earlier days of his complaint the pain, although related to food, was interscapular and not epigastric.* There was also a history of typhoid fever 14 years before the first development of symptoms.

CASE 2. *A case in which the severity of the pain led to a diagnosis of gall-stones and a fruitless operation; in which a radiologist later diag-*

nosed lesser curvature ulcer; but in which the clinical analysis led to a correct diagnosis of 'chronic posterior duodenal ulcer adherent to the pancreas'.

A fine old soldier of 73 had suffered from periodic bouts of epigastric pain for more than 6 years. Latterly these had become more severe and incapacitating. In the attacks he 'shook all over' and the pain compelled him to cry out. He saw a surgeon who diagnosed gall-stones, and notwithstanding a negative cholecystogram and a failure to discover stones at the operation he elected to drain the gall-bladder. After the operation the pain returned and was as bad as ever. I then saw the patient and made the following entries in my notes: *At an earlier stage the pains came at a long interval after food and were relieved by food. They were more troublesome at night. The pain in the bad attacks now goes through to the back at the same level on the right side, i.e. at the level of the 11th or 12th rib and not at the scapular angle. There was slight guarding with deep tenderness at the duodenal, not at the gall-bladder point. Finally, during convalescence from the operation, he had twice had melaena.* Clearly this last symptom made it very much easier for me, but I also had the good fortune to be familiar with the excessively severe pain of this type and distribution which may accompany a 'posterior ulcer adherent to the pancreas', and entered this as my diagnosis accordingly. I had him X-rayed and the radiologist found a spasmodic deformity strongly suggesting a mid-gastric ulcer. There was no response to medicine or diet. I therefore asked Mr. L. Bromley to operate. He found a posterior duodenal ulcer attached to the pancreas and no gastric ulcer. A gastro-jejunostomy was performed. In spite of his years the patient did well, after a stormy passage, and has remained fit subsequently.

CASE 3. *A case of aortic disease with abdominal angina subjected to alimentary tract investigations.*

A man, aged 55, with a history of 'valvular heart disease' first recognized 12 years previously began 8 years later to experience a 'grinding pain' around the navel. This was invariably induced by walking, especially up a slope, and it 'pulled him up'. He also had another pain shooting in character and radiating up towards the xiphisternum. This would waken him between 2 and 4 a.m., and he found that by sitting up and eructating he obtained relief. In the next year he was very fully investigated from the gastro-intestinal point of view, but the only conclusions transmitted to him were that he had colitis and a dropped colon. No treatment for his cardio-vascular disease was prescribed. I saw him a year later with symptoms and signs of commencing heart-failure. With the onset of dyspnoea and general weakness the pain on walking had disappeared, but the night pains were more troublesome. The first pain was undoubtedly anginal. The second pain, it seemed to me, might well

have a vascular basis too and be dependent on changes affecting the visceral branches of the abdominal aorta. He died within a few months.

CASE 4. *A case in which opinions as diverse as coronary thrombosis and gall-stones were entertained by different observers.*

I was consulted by a man in the fifties who gave me the following story. Ten weeks previously he was taken at his work with a terrible pain in the chest which was 'one great box of ache'. He wished he were dead, and for a time fainted with the pain, which did not leave him for 4 hours. The pain had started under the right breast, passed across the sternum to the left shoulder and down the left arm. He was seen in the attack by a doctor, who regarded the symptoms as anginal and gave him amyl nitrite and morphine with little relief. Eventually he was taken home. The pain did not leave him till the next day. He was pyrexial for several days and was seen by his own doctor, who on the strength of resistance and tenderness, and 'something coming up against the palpating hand' under the right rib margin, made a provisional diagnosis of cholecystitis and gall-stones. This doctor had the advantage of seeing him during his illness and I did not. Respecting each other's opinions we have agreed to differ, but perhaps I may give the further evidence on which I based my diagnosis of coronary thrombosis. Firstly, I ascertained that for a year past, and especially in cold weather, he had experienced an ache across the chest when he walked after a meal. A meal without a walk and a walk on an empty stomach did not produce this effect. These symptoms had been more severe shortly before his grave seizure. Secondly, since the seizure he had found that he could not climb stairs without the old ache. Thirdly, undressing in my presence caused slight dyspnoea. Fourthly, his heart-sounds were faint and equalized and his blood-pressure was low for his age and type, 105 systolic, 80 diastolic. Fifthly, he had had attacks of intermittent claudication and the posterior tibial artery was thickened in further evidence of the existence of vascular disease.

CONCLUSION

It is a criticism sometimes levelled at the clinician that *his work is regrettably unscientific. In general the criticism* may seem justified, and we know well enough that we cannot make of bedside medicine an exact sort of science. But in particular it is indisputable that a careful clinical examination or inquiry is just as much a scientific procedure as any other measure of research. According to Huxley's definition, 'Science is nothing but trained and organized common sense'—a definition which we should be

very ready to accept, and which applies particularly well to clinical work.

We hear much talk at the present day of research in general practice. I marvel at the temerity of anyone who can suggest that the busy practitioner should add another burden to his arduous life; but if there is one way of research not involving too great a consumption of time, and open alike to the general practitioner or to any other branch of the profession, it is that of keeping very full clinical notes on selected cases with a view to the solution of a selected problem in symptomatology. No symptoms better lend themselves to such a process of inquiry than some of the common pains of daily practice. A series of cases of headache, backache, or abdominal pain, as fully investigated as circumstances will permit, and carefully followed through the years, will certainly provide individual rewards for their investigator, and may ultimately furnish the material for a reasoned contribution to morbid physiology. System and patience are necessary, together with an inquiring mind. The only essential apparatus for the research is a good card index.

IV

VISCERAL PAIN AND REFERRED PAIN[1]

THERE are problems in medicine which make a general appeal, and others of a more special character which cannot equally attract all minds. In choosing for discussion certain aspects of pain, I have hoped at least to avoid the imputation of specialism, for it would be difficult to conceive a problem more universal and more appropriate to our art. Whether our inclinations be medical or surgical, or our thoughts cast in a physiological or an anatomical mould; whether our work be academic or more severely practical, there are features of the problem which can hardly fail to claim attention. To seek out the causes, to assess the consequences, and to encompass the relief of pains is for most of us a daily duty. Familiarity cannot—or should not—deprive the subject of its fascination or blind us to its difficulties.

If there is a fault in us bred of familiarity it is, I believe, the old fault of omitting to probe sufficiently deeply into causes; the fault of accepting the fact of common symptoms without trying to explain them. For this reason my remarks will be confined to a review of the present state of our knowledge of the nature and causes of some more familiar types of pain. Research into the subject does not commend itself to the experimentalist in the laboratory, for subjective phenomena are difficult to pursue in animals, and the varieties of pain which can be reproduced and studied in the healthy human being are of necessity limited. On the other hand, those who are engaged in the practice of medicine or surgery, and have the most frequent opportunities of observing the experiments in pain with which Nature herself provides us, are usually so harassed by the exigencies of work that ordered observations are hard to accumulate and still more hard to analyse. Furthermore, the experiments often take months or years to march to their conclusion,

[1] *Lancet*, 1926, i. 895.

and only too frequently they are not concluded at all. I think, however, it may fairly be urged that we owe—as we should do—our most valuable information relating to the mechanism and distribution of pains to the clinicians, and that it should rest with them to direct inquiries in the future, employing ever more careful methods, and seeking scientific co-operation whenever possible. With the work of such men as John Hilton, James Mackenzie, and Henry Head to reflect upon we do not lack for inspiration in this country.

It is with some diffidence that I approach the subject of local pain and referred pain in visceral disease, for if the more superficial pains are difficult to elucidate the deeply seated pains are more so. Moreover, the ground which must be covered is wide and beset with controversies. I shall confine myself to a consideration of pain associated with disease of the hollow viscera, for it is doubtful whether the solid viscera are possessed of any sensibility. My argument will be mainly clinical, and I must pray the physiologists and anatomists for leniency whenever my remarks seem to lack that precision which their more ordered sciences demand.

The Mechanism of Visceral Pain

To begin with, let me recall that there have been two main schools of thought in regard to the mechanism of a visceral pain. The first school, basing its views on the work of Lennander [1] and having the late Sir James Mackenzie [2] as its most vigorous protagonist, concludes that pain is not felt in the viscera, but that it is referred to the somatic tissues supplied by the same segment of the cord which supplies the viscus in question. The latest edition of a well-known physiology text-book still perpetuates this view. The second school, supported by Ross [3] and Hurst [4] and perhaps the majority of physicians, while recognizing that visceral disease may be accompanied by referred somatic pain, contends that the viscera themselves are capable of feeling pain in the presence of appropriate stimuli.

1. That there is a true visceral pain felt by the viscus.
2. That visceral pain is commonly due to an abnormal increase in the tension of the muscular element of the wall of the viscus, this increased tension resulting either from contraction or from a failure on the part of the muscle-fibre to relax adequately in the presence of increased intravisceral pressures.
3. That visceral pain when occurring alone, or dissociable from attendant somatic pains, may be accurately localized by the patient.
4. That referred somatic pain and tenderness—e.g., the viscero-sensory reflexes—and the associated viscero-motor reflexes, although they may accompany a severe visceral crisis of mechanical origin, more frequently express an inflammatory lesion of the viscus.
5. That, when persistent, they invariably express organic disease of the viscus of an inflammatory kind.

I shall illustrate my remarks by referring to painful disorders of the stomach, the gall-bladder, the appendix, the intestine, the kidney and ureter, the uterus and Fallopian tubes.

Normal Sensibility of Hollow Organs

If it be claimed that visceral pain is not produced in the viscus it seems pertinent to inquire where the normal sensations peculiar to certain viscera are felt. I have never seen it suggested that these normal sensations are referred to the somatic tissues, nor does daily experience suggest that they are felt elsewhere than in the viscus. The heart and aorta, excepting for the sensations of praecordial fullness and retrosternal oppression experienced during violent effort or emotion, may be said to be insensitive under physiological conditions. In the case of the stomach we recognize the gastric elements of the appetite and hunger sensations, and the sensations of fullness or repletion. These have been clearly related with the tonic and peristaltic activity of the stomach wall, and the work of Carlson [5] and Hurst [4] would seem to indicate that the sensations depend on the

state of tension in the gastric muscle-fibre. Of the appendix and gall-bladder we are quite unaware in health. Of the intestine we are aware whenever local distension with flatus occurs. The rectum clearly appreciates states of fullness, at times of urgency amounting to pain, and most of us would agree that its sensations are deeply and not superficially situated. The sensation of the desire to micturate is felt in the urethra and in the bladder also when it is overdistended. All these physiological sensations are related to increasing pressure on the walls of the viscus and are relieved by evacuation. Menstrual pains are felt locally, but are frequently accompanied by a more superficial sacral pain. It is, however, worthy of note that a state of congestion akin to the effects of inflammation is present in this condition in addition to increased muscle tension, and that no equivalent congestion is present during the normal functional activity of other hollow viscera.

Lennander [1] showed that the abdominal viscera when exposed could be pricked, pinched, cut, or burnt without causing pain, and we are all familiar with the insensibility to these stimuli of a colotomy loop. Waugh [6] has shown a similar insensibility in the case of the heart. It is further obvious that the gastric and intestinal mucosa have no tactile and very little thermal sensibility, for if they had, we should be far more conscious of ingested foods and fluids, of enemata, and of the normal processes of digestion. Hurst [4] and his collaborators demonstrated by experiment the insensibility of the gastric and rectal mucosa to tactile, thermal, and chemical stimuli, and Hilton [7] long ago remarked on the insensibility of the rectal as compared with the anal mucosa. These observations support the contention that, if the hollow viscera are sensitive, it is not their serous or mucous coats but their muscular coats which appreciate the sensations. Those who contend that the viscera are insensitive seem to have paid too little regard to the fact that special organs respond only to special stimuli. Thus the eye appreciates light and not sound; the skin appreciates touch, temperature, and traumatic pains, all of which it is physiologically essential for it to appreciate;

the skeletal muscles appreciate position and tension and the strength of opposing forces and (in states of extreme tension) pain, but they are not, I believe, sensitive to cutting, pricking, or burning. There is no reason for the hollow viscera below the gullet to appreciate tactile or thermal stimuli, but it is vitally necessary for them to appreciate states of fullness and emptiness. By analogy it seems reasonable to insist that the plain muscle of the hollow viscera is endowed with the same sensibility, positive and negative, as the skeletal muscles; in other words, that *visceral sense is muscle-sense*. The sensations of fullness or emptiness are thus parallel with the sensations of posture and tension in a limb. Pain (whether in skeletal or plain muscle) results when tension is greatly exaggerated in one manner or another. The common factor present in all cases of visceral pain is an increase in muscular tension or, perhaps (to conform with Lewis's work on angina), the ischaemia, and the associated chemical changes accompanying an increase in tension. The relieving factor, whether it be the passage of a gall-stone in biliary colic or the ingestion of food in hunger pain, is a factor which reduces tension in the wall of the viscus.

What further evidence have we that visceral pain is deeply felt and not somatic? It will be agreed that ordinary stomach-ache and intestinal colic give the impression of being felt internally. Those who have experienced severe visceral pains of mechanical origin, such as renal and biliary colic, are agreed that these sensations seem to be deep to the body wall. I think it is also true that the majority of non-inflammatory visceral pains (unless they fall into the group of the severe visceral crises) are but rarely accompanied by reflected superficial pain or soreness, and in the case of inflammatory lesions we may observe, as I shall show, referred somatic pain or tenderness occurring in the absence of local visceral pain, and thus suggesting that the causal processes are not identical.

Guarded though we should be in accepting the observations of our patients as accurate evidence, we must, nevertheless, attach importance to certain 'gestures' which they employ in indicating the seat of their pain. These gestures

do not, as a rule, apply to a somatic segment, but to the surface-marking of the viscus. Thus, in describing anginal pain the patient places his clenched hand to the sternum as though to indicate a median or cardiac origin for his pain, and, perhaps, incidentally, to imply its gripping character. The pain of gastric ulcer is indicated with the tips of two or three fingers applied to the mid-epigastric point or occasionally just to the left of this point; the pain of duodenal ulcer by a similar demonstration frequently just to the right of the mid-line. The gesture of renal colic is made familiar by the pictorial advertisements of a certain proprietary back-ache pill; the hand grasps the loin usually with the fingers over the back and thumb in front, as though to imply that the pain requiring subjection is rather more posterior than anterior and deeply situated in the actual position which the kidney occupies. The localization of pain in gall-bladder and appendicular disease (when there is no confusion due to associated inflammation or gastric and intestinal disturbance) is remarkably accurate. The position of a calculus impacted in the ureter may also be accurately shown when distraction by concurrent renal colic or other symptoms is not too strong. Intestinal pains are less easily localized, but here the actual position of the painful contraction is variable, for intestinal colic is not confined to one spot as is the case with biliary or renal colic. Small intestine pains are usually felt around the navel, and colonic pains between the navel and the symphysis pubis. When, however, obstruction occurs at a more or less fixed point, such as the hepatic, splenic, or sigmoid flexures, then the localization is commonly precise. One of the most recent text-books of physiology, in the very brief references to this subject which it makes, asserts that visceral pain is vaguely and inconstantly localized. I believe that clinical experience teaches otherwise, if only we are careful to dissociate the primary or local from the secondary and referred phenomena.

It will be conceded that the reflected phenomena of visceral disease are best demonstrated in association with the very severe forms of visceral pain or in association with

inflammatory disease. The arm pain of angina, the subscapular pain of cholelithiasis, and the testicular pain in ureteric colic are the classical examples of the former group; of the latter the cutaneous hyperalgesia and muscular guarding found in appendicitis or in relation to a chronic gastric ulcer are the best examples. It is worthy of note that these reflected phenomena rarely accompany visceral disease of a functional kind; in other words, that they are generally associated with local organic changes. In stomachache due to extragastric causes I have not found cutaneous soreness or muscular guarding. With the subscapular pains of gall-stones it may be pleaded that the pain is as much an effect of the cholecystitis as of the stones; certainly an identical subscapular pain occurs in cholecystitis without gall-stones. In the testicular pain of calculous ureteric colic the ureteric mucosa must frequently be ulcerated or inflamed and testicular pain may occur without any attack of 'colic'. It is upon observations of this kind that we may base the conclusion that *visceral pain expresses a perturbation of visceral function (which may or may not be due to local organic disease), while the somatic phenomena generally express a structural lesion of the wall of the viscus.*

Gastric Pain

My interest in the subject of visceral and referred pain was first stimulated by studying cases of gastric and duodenal ulcer. The pain of duodenal ulcer, usually gnawing or aching or described as a feeling of great pressure, occurs when the stomach is in the posture of approaching emptiness, but, through reflexly enhanced tonic action, its muscle becomes and remains abnormally taut. This pain is relieved when the stomach adapts its posture or relaxes to accommodate introduced food or fluid, or when the 'resistance' is withdrawn and intragastric pressure reduced by complete emptying. The pain of gastric ulcer occurs when the tension in certain muscle-fibres, reflexly tautened or structurally shortened by the ulcer, is further augmented by the introduction of food. In cases of ulcer we are frequently told by the patient that these spontaneous pains are accompanied

and often followed by local epigastric soreness or hyperalgesia. In a large proportion of cases we discover deep somatic tenderness. In a much smaller proportion we find superficial and deep hyperalgesia (or soreness) of the skin, together with muscular guarding of one or other rectus and exaggeration of the abdominal reflex on one side. These signs are more likely to be demonstrable if the patient has recently had an attack of pain or is in pain at the time of the examination. On the other hand, these signs may persist for days after the subsidence of all spontaneous pain as the result of appropriate treatment in bed, and they may not finally disappear for a week or fortnight. The purpose of these reflexes is surely protective, so why should they only be present when spontaneous pain is present? They disappear completely when the ulcer is healed, as judged by the disappearance of occult blood from the stools, and they are not present in cases of established pyloric stenosis. They are, therefore, probably due to stimuli constantly passing from the ulcerated area to the cord, and, although they may be brought to light or reinforced by them, are not directly attributable to the painful contractions in the stomach wall which cause the visceral or deeply seated pain. These reflex signs are more constantly present with the deeper and more chronic ulcers which invade the muscular coat. Although the pain of cancer of the stomach may equal or surpass in severity the pains of gastric ulcer, it is much more rarely accompanied by somatic signs. Thus, while it is difficult to palpate deeply in many ulcer cases on account of somatic tenderness and muscular guarding, in cancer the muscles are often relaxed and the tumour can be felt without causing flinching or pain. I believe this apparent discrepancy may be related to the fact that simple ulcers erode and destroy the muscle-fibres in which the nerve-endings ramify, whereas the growth merely infiltrates between the fibres—an histological distinction which is regarded as of diagnostic import by pathologists when considering the nature of large chronic ulcers. When 'guarding' is present in cancer of the stomach it is usually bilateral and evidence of peritoneal involvement; in gastric ulcer it is usually left-sided,

and in duodenal ulcer right-sided. Pain is referred to the back over the lower ribs, particularly in the case of posterior ulcers eroding the pancreas. Somatic signs are rarely present in simple gastritis, because the lesion is too superficial and does not involve the muscular layer. The following cases illustrate some of the points to which I have referred.

CASE 1. J. D., male, aged about 50, was diagnosed clinically and with the aid of X-rays, test-meal, and the presence of occult blood in the stools as having a duodenal ulcer. On admission to the ward he had deep cutaneous soreness, deep tenderness over the right upper rectus, and the abdominal reflex was exaggerated in the right upper quadrant. The deep soreness was very marked and at times superficial soreness was also present, the patient volunteering the statement that the weight of a book as he read in bed and even that of the bed-clothes was sometimes insupportable. The signs persisted for some time after he lost his pain, but then gradually became less and less distinct. *Deep tenderness was the last sign to disappear, and its complete disappearance coincided with the return of negative occult blood reports from the clinical laboratory.*

CASE 2. A young man, aged 27, was diagnosed as having a gastric ulcer at out-patients and the X-ray report confirmed, stating that there was a penetrating ulcer of the lesser curvature. On his first attendance he was free from pain and the only sign demonstrable was deep mid-line tenderness in the epigastrium. On his next visit he was actually in pain, and he showed, in addition to the mid-line tenderness, deep cutaneous soreness in the mid-line, left-sided exaggeration of the abdominal reflex, and left-sided guarding.

It is very rare in my experience for superficial soreness, elicited with the head of a pin as Head [8] described, to be present in gastric disease. In distinguishing between a gastric and a duodenal ulcer the horizontal level of tenderness is less reliable than the right- or left-sidedness of the viscero-sensory and viscero-motor signs.

PAIN IN GALL-BLADDER AND BILE-DUCTS

The pain of biliary colic is referred to the gall-bladder point, corresponding with the ninth costal cartilage, or sometimes more centrally below the xiphisternum. It is almost invariably a crescendo pain. It is often difficult to dissociate the attendant gastric pain from the true gall-bladder pain. In association with gall-stones and chronic cholecystitis it is not uncommon to find a recurrent gastric

pain, often worse at night, simulating the pain of ulcer and dependent upon similar reflex disturbances of gastric motility. The viscero-sensory accompaniments of cholecystitis—whether occurring with or without gall-stones—include superficial and deep soreness in the right upper quadrant of the abdomen, right subscapular and interscapular pains, and tenderness over the middle dorsal spines and along the course of the eleventh right rib. Muscular guarding, amounting in acute cases to actual rigidity, may also be present, and, in subacute cases, exaggeration of the abdominal reflex on the right side. 'Shoulder pain', so often referred to as a sign of gall-stones, should be reserved for the description of pain referred along the phrenic nerve to the C4 area in cases of inflammation involving the under surface of the diaphragm or in diaphragmatic pleurisy. It is best seen in liver abscess and subphrenic abscess and is sometimes an early symptom of a perforating gastric ulcer. I have never met with it in uncomplicated gall-stones or cholecystitis. I shall here give the notes of one case only, that of a medical man, who helped me with careful observations.

Case 3. The patient first came under observation on account of severe attacks of epigastric pain of unexplained causation. At the time of investigation he was free from all symptoms. A week spent in thorough investigation by the various modern methods failed to clear up the diagnosis. *The only positive sign was slight tenderness over the fifth and sixth dorsal spines, and the possibility of gall-stones was on this account considered.* A few weeks later I saw him in an attack with a palpable gall-bladder and, on the following day, a rigid right upper rectus and friction sounds below the rib margin. At operation a very much thickened and inflamed gall-bladder filled with stones was found. Some months after the operation he had one further attack of biliary colic, perhaps due to a stone left in the dilated duct. Later still I saw him with troublesome referred pains in the mid-dorsal region unaccompanied by abdominal colic or epigastric pain. I thought that these pains were due to persisting infection in the dilated ducts, and with hexamine the symptoms were at first relieved. Later, however, they recurred and hexamine failed to bring relief. The patient has since written to me in the following words: 'One day it occurred to me that this pain was purely a dragging pain and might be due to inability of the liver to get rid of its secretions through a kinked duct. I decided to sleep on my left side. I could not do this

before, but the difficulty was overcome. The effect was excellent. I never get that pain now unless I happen to turn on my right side, then it comes next day. I have tried the trick again and again and there can be no doubt of cause and effect. . . .'

It is difficult in this case to decide how far the referred phenomena should be regarded as an effect of inflammation and how far as an effect of mechanical distention of the ducts. In the first instance they were seemingly relieved, as I have seen them relieved in other cases, by treatment directed towards disinfection of the biliary tract. Latterly they were relieved by a simple expedient likely to facilitate evacuation of the duct. Perhaps it is fair to suggest that both factors played their part, just as mechanical and inflammatory factors are shown to buttress one another in promoting the somatic signs of gastric ulcer. Hilton [7] was the first to give an anatomical explanation for the frequent association of subscapular and interscapular pain with diseases of the upper alimentary tract, pointing out the connexions between the nerve supply to the stomach, liver, duodenum, and pancreas (great splanchnic and solar plexus), and the fourth, fifth, and sixth dorsal nerves.

Appendicular Pain

Among the varieties of disease collected under the heading of acute appendicitis there are two broad clinical types which it is essential to distinguish. The first is the 'inflammatory type' in which, following upon infection of the mucosa or submucosa, there develops general redness and inflammation of the organ with or without obvious pus formation. In this type, in addition to visceral pain, cutaneous hyperalgesia, muscular guarding or rigidity, and pyrexia are commonly present. If reflex signs are carefully sought for they may be found in some of the mildest and earliest cases in which it might otherwise be difficult to arrive at a diagnosis. The second type is the 'gangrenous' appendix, which may give rise at first to exceedingly severe visceral pain, but not infrequently with a complete or almost complete absence of somatic signs and pyrexia. In the absence of these signs the diagnosis is sometimes un-

happily postponed, and yet it is the type above all others in which early operation is imperative. In either type there may be a sudden disappearance of the visceral pain when the appendix ruptures—a strong point in support of the contention that visceral pain is an effect of increased tension. In the gangrenous type we have a lesion in which not only the lumen but also the circulation of the organ has become obstructed. Possibly the absence or paucity of somatic signs in these cases may be explained by the mechanical nature of the lesion in the early stages and by the ischaemia of the tissues involved in the later stages.

CASE 4. A medical student, aged 22, came to me some years ago with the following history: Three months previously he had had a sudden attack of pain in the epigastrium which later settled into the lower abdomen. He stated that there was tenderness on the right side and round the navel, that he vomited, and that his temperature rose to 99·4° F. Forty-eight hours later he was quite well. He remained fit for a month and then had a similar attack in which there was pain and tenderness in the epigastrium. Ten days before he saw me he had had a third attack which started absolutely abruptly at 8 p.m., with pain in the epigastrium which doubled him up and made him feel cold. At 10 p.m. the pain departed with absolute suddenness under the following circumstances. He was on his way home to his rooms and met a registrar from the hospital who told him how ill he was looking. He said: 'Yes, I have a bad stomach-ache. . . . No, I have not, it has gone.' At no time had the pain been referred to the back, or groin, or testicle. Between the attacks he was perfectly fit in every way, and at the time of his visit to me he was quite free from symptoms. My physical overhaul was completely negative except for showing local deep tenderness at McBurney's point. A radiographic examination of his alimentary and urinary tracts was negative. Bastedo's test produced no localized pain. A week later all tenderness had disappeared and he felt perfectly well. I regarded the attacks as probably appendicular, and told him that at the first sign of any recurrence he was to come up to the hospital. As it happened the next attack started in the middle of the night, the pain was of great severity, and he could not attract the attention of anyone in the house. He came to see me in the morning looking pale and ill. There was no pyrexia, no cutaneous soreness, no rigidity, and only very slight tenderness in the right iliac fossa; the pulse was not accelerated, but as he lay on my couch he preferred to do so with the right knee drawn up. I had him admitted to hospital at once, and Mr. R. P. Rowlands removed a black gangrenous appendix. At its proximal end there was a small thorn impacted in the lumen of the

organ. Although appendicular disease seemed more probable, the curiously abrupt onset and departure of pain in the early attacks and their epigastric reference had made me consider the alternative possibility of one of the major colics. With such a history before me now I should not dare to await events.

Intestinal Pain

Intestinal pains are generally griping and rhythmically recurrent, but with partially obstructive lesions in the large bowel the pain may be more sustained. Excepting with ulcerative or inflammatory lesions it is unusual to find cutaneous soreness or muscular guarding in intestinal disease. These signs may be present with tuberculous ulceration of the ileocaecal region and with diverticulitis of the colon, but they are rare in mechanical obstructions and in cancer. Head [9] points out that they may be present in typhoid fever, but are absent in lead colic, yet another observation in favour of the suggestion that visceral pain is an effect of muscular tension, while for referred pain or tenderness the added effect of inflammation is necessary.

Renal and Ureteric Pain

One of my most instructive lessons in visceral pain and referred pain was provided by a personal experience of renal colic. I must apologize for referring to this experience and should hesitate to do so did I not believe that personal records by medical men have a certain value of their own.

Case 5. In February 1922 I began to have attacks of left-sided renal colic and between then and July of the same year, when I passed a small calculus, I had four or five major attacks and about a dozen minor ones. I was satisfied that both the renal pain, which was always crescendo in character, and later the ureteric pain were deeply situated. At an intermediate stage the latter appeared to me to be just deep to the sacro-iliac joint, but shortly before the stone passed into the bladder it was felt low down in the left iliac fossa. One bad attack was relieved by morphine and atropine when morphine alone had failed. I was told by a colleague that my loin muscles after attacks of renal pain were hard on the affected side and they certainly remained tender for a day or two, after the manner of a muscle which has been over-used. Jolting and gentle thumping of the loin were painful, but deep palpation caused no discomfort. At no time did I discover any cutaneous hyperalgesia. There was frequent

referred pain into the left testicle during the long period in which the stone was lodged in the lower end of the ureter, and this occurred quite independently of ureteric or renal crises. There were several bouts of haematuria, and red cells and latterly leucocytes were always present in the urine when examined. It seemed to me that the referred testicular pain was an effect of local ulceration of the ureter, although its intermittency suggested that ureteric peristalsis played a contributory part.

I have not encountered testicular pain in cases of renal colic due to an aberrant vessel, and I do not think it occurs in cases of stationary stone in the kidney. It is therefore to be regarded as a ureteric and not a pelvic or renal reference.

Uterine and Tubal Pain

The number of obstetric and gynaecological cases which comes my way is small, and I have few opportunities of studying their pains. As with dysmenorrhoea and parturition, so with organic disease of the uterus, back-ache in the sacral area is a common association. Pain down the front of the thigh to the knee, in the area supplied by the eleventh and twelfth dorsal and first three lumbar segments, is an interesting reference accompanying disease of the pelvic organs which I have encountered once or twice, and which Marcus [10] has particularly associated with disease of the tubes, citing several cases of salpingitis and ectopic gestation. Head [11] had concluded that the eleventh and twelfth dorsal and first lumbar were the segments involved in certain uterine cases. Hilton [7] long ago suggested that some of the so-called hysterical pains in the hip and knee might depend upon reference from the pelvic organs, and traced the path of the impulses via the sacral and lower lumbar ganglia to the sacral nerves and obturator.

Practical Applications of the Study of Pain

Thus far my remarks have been chiefly concerned with an attempt to support (in the case of each viscus) the hypotheses set forth at the beginning of this lecture. Truism though it may seem, it is now time to remind ourselves that a working knowledge of the causes of symptoms is of great practical importance, perhaps of even greater importance

to the physician than a knowledge of the causes of disease. Of all symptoms pain is the most important. In the earlier stages of our education a great deal of time was and still is quite properly devoted to the study of physical signs—that is to say, of the objective evidences of structural disease. But symptoms, being invisible and impalpable, are too often thought to be poor material for class demonstration. In practice we find that only a small proportion of our cases have physical signs; that the development of signs is nearly always preceded by a period of symptoms; and that again and again we have to base our findings on the anamnesis rather than on the physical examination. It thus becomes necessary for us to educate ourselves in methods of analysing pains as accurately as possible, in collecting information about their character, situation, and attendant phenomena, and the factors by which they are intensified or relieved. We have, no doubt, been taught that certain pains have certain degrees and qualities; that the severe crises like angina and renal colic are 'agonizing' and 'unbearable'; that the 'spasmodic' types of pain, as Heberden [12] remarked, are peculiarly liable to come on in the middle of the night or the early hours of the morning; that pain in the lateral organs does not as a rule cross the mid-line; that intestinal pains, like the normal peristaltic movements of the intestine, are rhythmical; that certain pains are constantly relieved by certain acts, such as the pain of duodenal ulcer by taking food; that cardiovascular pains accompany effort; that gastric pains are related to eating or fasting. Later we discover for ourselves that many other pains and discomforts, previously but dimly understood, may have their nature revealed by careful analysis, although the most experienced of us must again and again admit defeat. With hospital patients, and with private patients who can afford such luxuries, it is now possible to subject the more puzzling problems to fuller investigation and so to correct or modify an original clinical opinion. The possession of these new facilities should never, however, excuse us from careful clinical inquiry. The 'pathology of the living' studied on the operation table is also a valuable corrective, but opera-

tion should rarely be resorted to for purposes of diagnosis. One of the most important things in studying pain is to endeavour to see the patient when the pain is actually present; in certain circumstances, in order to assist diagnosis, it may even he justifiable to take steps to reproduce tbe pain. It is remarkahle how rare are the opportunities in tbe medical wards of a hospital and in eonsulting practice for seeing the patient during a hout of pain. Even in general practice the patient often prefers, or is compelled, to seek advice between attacks unless he he very gravely smitten.

A technique of interrogation, involving ten questions and aimed at making our knowledge of an individual pain more precise, was outlined in the previous lecture. In addition to the usual routine overhaul an examination for the presence or ahsence of referred signs should always be made in doubtful eases, and this is particularly important in dealing with acute or chronic abdominal disorders. The difficulties with which we have to contend are manifold. They include the limited powers of observation and description possessed hy many patients; the 'spread' or exaggeration of certain pains in nervous or dehilitated subjects; the minimization of pain hy others; and last, but by no means least, the shortness of life in comparison with thc length of our art. In general practiee there are better opportunities for seeing patients repeatedly, of observing minutely variations in the behaviour of their symptoms, and of assessing individual physical and psycbological reactions to these symptoms. Those of us whose work is of a consulting kind may, on the other hand, have better opportunities for special investigations, for study in the post-mortem room, and for discussion of problems with colleagues. For all of us the surgeon, thc specialist, and the pathologist from time to time will furnish proofs which have long been waited for, and occasionally a patient with unusual powers of observation may greatly illuminate some particular point of doubt.

Group Study of Pain

In conclusion, I should like to suggest that there is no study more likely to furnish interests and rewards in practice

than a concerted study of visceral or other pains. Results will come very slowly, but this need not discourage. No apparatus is required, no laboratory experience is necessary, and yet a valuable piece of clinical research can be pursued if four or more men in one town will set to work to keep and pool their notes of all cases of certain types of pain. Headaches or back-aches may be studied in preference to stomach-aches or heart-aches; or several varieties of ache may be simultaneously reviewed. Such inquiries must inevitably clear the mind on many points which were formerly obscure, and help to establish facts hitherto imperfectly established. And finally, even though time or inclination for special inquiry be lacking, each one of us can bear in mind a saying of Hilton's which I am never tired of quoting: 'Every pain has its distinct and pregnant signification, if we will but carefully search for it.'

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V

THE STUDY OF SYMPTOMS[1]

THE clinical appraisement of disease in man is customarily based upon inquiries into personal and family history and environment; the patient's account, both voluntary and elicited, of his own subjective discomforts; an estimate of his physical type and psychological endowments; and a routine examination of his various systems. In cases of doubt or difficulty we may further employ certain instrumental devices such as the electrocardiograph, or invoke the aid of the radiologist, the chemist, or the bacteriologist. Where none can be neglected it would be difficult indeed to say upon which department of such an inquiry we chiefly rely for our opinions. In one case the patient's ancestry or his own previous pathological career may be all-important, in another physiognomy, or the physical examination may give the answer to our question. Often a judicial analysis of all available information is necessary. In the earlier part of our clinical training it is usual to stress the importance of physical signs, and long hours are properly devoted to practising the arts of palpation, percussion, and auscultation. Nevertheless I am persuaded that with the growth of experience pride of place should be given to symptoms—that is to say, to the purely subjective phenomena of disease. Without symptoms patients would not come to us at all. Symptoms are a part of morbid physiology; they express disturbances of function. As a rule, therefore, they precede the development of signs which are but the outward morbid anatomy of the living.

In the first days of practice we are often baffled by the symptoms which our patients describe, and sometimes disconcerted when we find so little of an objective nature to support or explain them. As the years go by, however, we begin to understand and to be grateful for symptoms. Again and again we find ourselves making a reasonable diagnosis

[1] *Lancet*, 1931, i. 737.

while we sit and listen to the patient's story or ply him with our questions, before ever his clothes have been removed or a physical sign has been sought. The majority of patients have indeed little to show in the way of physical signs, for these depend upon advanced structural change. But even in serious forms of organic disease in which, sooner or later, definite physical abnormalities become apparent, symptoms may not only be earlier but also more eloquent than signs. They have, therefore, a particular value for the contributions which they make to early diagnosis. And so, on the score of its practical utility alone, I hope you will bear with my attempts to interest you in a subject which might at first seem to be an elementary part of the daily task of all students of medicine.

There is, however, another aspect of symptomatology, and that is the attraction which it offers as a study in itself. For many of us the philosophy of medicine, which runs parallel with the art of medicine pursued for humane ends and with a view to 'bread and butter', is a perpetual interest. I am sure we should endeavour to make it so, for the joys of practice are greatly enhanced if we can also gather in our work some of the crumbs of the philosopher or the natural historian.

I shall therefore commend to you the study of symptoms for their own sake as well as for the sake of your patients and your professional reputations. I do so the more eagerly because I feel that the subject still suffers neglect in our generation and that it offers a wide field for future research.

Methods of Study

Two important papers appeared during 1931 in the *British Medical Journal*, one by Sir Thomas Lewis entitled 'Research in Medicine: Its Position and its Needs', and the other by Mr. Wilfred Trotter entitled 'Observation and Experiment and their use in the Medical Sciences'. The first is critical, stimulating, even provocative, and makes an appeal on behalf of clinical science as distinct from curative medicine. It suggests that the experimental study of disease in man, as

supplementary to the older observational method, must shortly come into its own and appeals for the appointment and endowment of research physicians who shall be relieved of the necessity of practice. The second is an admirable philosophical inquiry into the relative merits and achievements of the observational and the experimental schools. In the biological sciences it is clear that observation and experiment must ever go hand in hand. The great clinical scientists have commonly made use of both. It is certain that experiment will play a fuller part in the future, but observation must continue to make its steady contributions to knowledge. It should be our continual concern to train better observers and better experimenters. Now it is obvious that only a minority have the means, the aptitude, or the opportunity essential for the life of the experimenter. The majority will continue to enter practice in one form or another, and every one of these must do his best to become an observer, or in fact a physician—a student of φύσις or nature, for this (as Professor Gairdner[1] so aptly insisted many years ago) was the original interpretation of the word. The more correctly he observes and the more carefully he sifts and records his observations the better practitioner will he be, and the more likely is it that he will render useful service to clinical science. There is no subject that he will have better opportunities of studying than the subject of symptomatology, for he will live in the midst of symptoms. It will, I think, be a very long time before symptoms can be studied experimentally on any considerable scale. Very few of them can be accurately reproduced. The majority of them as they occur in nature are transient. We have no practical method at present of measuring or photographing subjective phenomena. They express the behaviour of diseased or disordered tissues, and, like the behaviour of plants and animals, we are likely to learn more about them by constant and close observation, by careful recording, and by correlation of these observations with objective phenomena and existing physiological knowledge than by any other process of study.

[1] *The Physician as Naturalist*, Glasgow, 1888.

If we pause for a moment to think of such familiar symptoms as pain and dyspnoea we realize at once that, while our intimate knowledge is slight, we can already classify them into several varieties of pain and dyspnoea and that in certain instances a particular variety has a very special significance. When it has a special clinical significance it also has a special physiological significance, and the actual mechanism of the pain or the chemistry of the breathlessness in such case has commonly been proved. In time it should be possible to sift and classify and analyse all the subjective phenomena of disease in the same way, and the meaning of nausea, heartburn, anorexia, the various forms of breathlessness, vertigo, the various headaches, back-aches, heart-aches, and stomach-aches, the referred pains, the dysurias and dysmenorrhoeas, the tinglings and numbnesses, the fidgets and the spots in front of the eyes, will then be made more clear to us. It can scarcely be disputed that diagnosis, prognosis, and treatment will greatly benefit thereby.

That our individual studies of symptoms may prove a pleasant task I shall endeavour to show out of my own small experience. At the same time I shall offer more detailed suggestions for the conduct of the observational method in this field.

Nature and Function of Symptoms

Symptoms, as has been stated, express a disturbance of function. Although they are often caused by organic disease they do not express the disease but the disturbance of function which the organic change produces. The same symptoms may thus be produced by functional error or structural flaw. While not specific for diseases, symptoms are, nevertheless, specific for functional errors, and these errors, for the most part, depend upon an exaggeration, a depression, or an inhibition of normal reflex phenomena. The dyspnoea of great effort in health is physiologically similar to the dyspnoea of small effort in heart disease. The angina of anxiety or tobacco excess or anaemia has the same physiological basis as the angina of coronary sclerosis, although none of its gravity. Gastric and intestinal pain as severe

as the pain of gastric ulcer or intestinal obstruction may occur in the absence of gastric or intestinal disease. It is by the character and behaviour of the symptom and by its associations that we differentiate. Giddiness may be due to cerebellar disease, to slight organic changes in the labyrinth, or to transient circulatory effects. Again it is not on the symptom itself so much as its severity, duration, and associations that we base our diagnosis.

The conception of symptoms as the signals of functional disturbance may seem a very elementary one, but it is none the less important. It is as such rather than as the listed characteristics of diseases that we should wish to view them. We should constantly be asking ourselves '*What does this symptom mean?*', not '*What is it a symptom of?*'

The function of symptoms is presumably protective. Dyspnoea demands general rest for a local and general advantage. Pain in an injured limb compels local rest and so permits repair. The pain of angina pectoris demands instant immobility and so spares the heart in jeopardy from anoxaemia and acute muscle failure. The pain of exaggerated hunger-tonus in duodenal ulcer calls for food-relief with temporary mechanical and chemical rest for the ulcer. The pain and short, shallow respirations of pleurisy and pneumonia limit the expansion of the chest and rest the inflamed pleura and lung. 'Pins and needles' in a cramped limb wake us from sleep and compel us to restore circulation and sensation by movement and friction. Often, we must confess, nature seems to overdo the protective stimulus, for pain may be out of all proportion to the size and gravity of the lesion. Thus the pain of a minute anal ulcer is excessively severe and, although the spasm of the sphincter may shut the canal against the passage of faeces, it is in itself a cause of added pain and by causing constipation may even aggravate the trouble. The protective significance of many other symptoms is obscure, but for the most part they are symptoms whose nature remains at present undetermined. In a more remote and less biological sense symptoms in man are protective in that they compel their victim to seek the advice and aid of others.

The remote physical symptoms of anxiety, hypochondria, and other psychic disturbances are of central origin or to be referred to the emotional plane. They may be due to a loss of balance between vagal and sympathetic activity, or they may be called into action as a mask for truth or as a plea for sympathy. It is also an early lesson of practice that the degree of symptoms primarily due to physical causes may be increased by anaemia, general debility, temperamental factors, or psychic states. Such modifications provide one of the most considerable difficulties encountered in the assessment of the subjective phenomena of disease.

Three Symptoms

I propose to review some elementary observations on three very diverse symptoms, all likely to be encountered in general practice or medical consulting practice, all capable of expressing organic change or functional disorder, but all —properly assessed—of the greatest help in distinguishing organic from functional disease.

The first symptom is a type of *abdominal pain originating in the colon*. Sometimes of considerable severity, it is one for which operations are frequently but fruitlessly performed. The suggested method of analysis of this pain may stand as an example for the analysis of any other visceral pain, and as one plan of attack in the observational study of subjective phenomena.

The second symptom is *nausea*. It is one which may be evoked in health and which occurs in a variety of physical disorders. The method of considering the common factor or factors in the widely varied conditions in which it occurs is another obvious method of approach to an individual symptom.

The third symptom is one of the strangest but apparently one of the most real and vivid of all subjective phenomena. It is the *sense of dying*, the *feeling of impending dissolution*, or *angor animi*, which in the literature is usually associated with angina pectoris but which also occurs in several other conditions, as I shall show, and most frequently in the absence of serious structural disease. This symptom being,

like nausea, less precise and definable than pain, requires other measures of analysis.

Colonic Pain

The particular type of abdominal pain on which these observations are based occurs as a rule in the absence of any demonstrable organic change and is the expression of tonic over-activity or sustained spasticity in the colonic musculature. It is frequently troublesome and persistent, sometimes very severe, and quite commonly leads to appendicectomy or exploratory operations. Here is an account of a case:

A man, aged 30, of spare habit and nervous temperament, first began to experience abdominal pains at the time of his final examinations in medicine. After a period of freedom they recurred when he sat for his final Fellowship. They were referred to the right side of the abdomen. Later he experienced them in the upper abdomen and occasionally he had pain in both iliac fossa. In the past he had suffered from asthma and migraine. When he first consulted me he had been examined with X-rays on no less than six occasions, and had been diagnosed as having both a hypertonic and a hypotonic stomach, and as a case of 'nerves'. Fatigue and worry were the chief aggravating factors. On one occasion he thought he had appendicitis, but then discovered that what he took for rigidity was a hardened caecum or ascending colon. I found a cord-like descending colon, and on another occasion an easily palpable and contracted ascending colon. With reassurance and modifications in his mode of life his health improved greatly. In his attacks he found that belladonna gave him great relief.

The condition has been variously described as spastic colon, spasmodic constipation, and tonic hardening of the colon. It is a visceral neurosis akin to asthma. Its aetiological characters are discussed more fully in Lecture XII; and its morbid physiology in Lecture XI. Anxious to investigate the nature of the disorder and the cause of the pain, I analysed my notes of 50 cases and applied to the pain itself certain tests or queries which have been helpful to me in the study of other pains. These tests or queries, already listed in Lecture III, are in the form of ten questions relating to: (1) the character of the pain; (2) its degree or severity; (3) its situation; (4) its localization or extent of diffusion; (5) its

paths of reference; (6) its duration; (7) its frequency; (8) its special times of occurrence; and (9) and (10) its aggravating and relieving factors. These are finally correlated with associated symptoms and objective phenomena.

The purpose of these questions is simply to make our knowledge of the pain more precise. Too often we are content with the patient's statements that he has a 'pain in his belly'. As anatomists, physiologists, and psychologists we should desire to know much more than that, and even if we are not dealing with measurable things we should, whenever time and opportunity permit, evolve methods of improving our standards of clinical accuracy.

The answers to these questions in the case of spastic colon are as follows:

(1) The *character* of the pain is a '*dull, steady* ache', *sometimes* gnawing and never 'griping' as in the peristaltic pain of purgation or obstruction.

(2) Usually 'bearable' it is occasionally so severe as to suggest one of the major 'colics'.

(3) Its *situation* is in the course of the ascending, the descending, or transverse portions of the colon, in this order of frequency. It may occur in one or more of these situations *simultaneously*. There may also be rectal pain.

(4) and (5) The *localization* corresponds accurately with the true surface marking or radiologically observed course of the colon. Sometimes it is more diffuse. *Referred pain* and *tenderness* in the somatic planes are rare.

(6) and (7) The *duration* of the pain may be for an hour, hours, or even days. *Its frequency is very variable and depends largely on* personal and environmental factors.

(8) A *special time of occurrence* is 2 or 3 hours after food, and of *non-occurrence* during the night when, with warmth and physical and mental relaxation, the pain usually departs.

(9) *Aggravating factors* include cold, fatigue, worry, constipation, purgatives, jolting, exercise, and tobacco.

(10) *Relieving factors* include warmth, holidays, belladonna, and large warm enemata.

Associated symptoms include constipation frequently and diarrhoea less frequently; dysmenorrhoea; urinary frequency; and 'dead fingers' in cold weather. The chief objective finding is o readily palpable and firmly contracted colon due to tonic rigidity, shortening, and straighteoiog of the

affected portion. The sigmoidoscope may show a sustained spasm synchronous with pain. An X-ray examination may reveal thread-like narrowing of the bowel lumen, straightening of the affected loop, and disappearance of natural haustrations.

From these and other observations it seems only reasonable to conclude that the pain itself is due to a sustained tonic contraction of the bowel, and that this depends upon an inherent irritability occurring in association with certain physical and temperamental types.

What are the practical and the philosophical advantages of such an inquiry? In practice it enables us with greater confidence and a diminishing margin of error to differentiate an important visceral neurosis from appendicular disease, duodenal ulcer, diverticulitis, carcinoma coli, renal and biliary colic, ovarian and tubal disease, and hypochondria. All of these at times have been alternative diagnoses in the minds of myself or of colleagues who have referred cases of this kind to me.

The philosophical value comes from the application of a definite method to a simple clinical inquiry and from the small increments of knowledge gained thereby. To the physiologist or the physicist the procedure may seem clumsy and lacking in anything savouring of exactitude, dealing as it does with processes which cannot be measured. Nevertheless their precise experimental methods would find no application at the present time in the solution of such a problem. To the field naturalist—and the physician is the field naturalist of medicine—the procedure might appear as a reasonable and appropriate attempt to improve the accuracy of the observational method.

Nausea

With a symptom such as nausea we are in greater difficulty for, although we understand quite clearly what we mean by nausea, we can scarcely describe it in the way that we can describe a pain. Even its localization is a difficult matter, and at present we must accept that it is felt in the pharynx and the epigastrium, sometimes more in one place

than the other, sometimes in both together. General sensations of malaise and faintness commonly accompany it. The symptom can be engendered in various ways in healthy people. Some are more sensitive than others, and women are more readily afflicted than men. A revolting sight or smell or even the thought or recollection of something unpleasant may induce it, and here it provides a good example of the conditioned reflex. The ingestion of greasy or fatty dishes, of paraffin or castor oil, or the smell of frying—all these particularly in hot weather, when the appetite sense is dulled—are familiar provocatives of nausea. Of foodstuffs it is particularly noteworthy that fats and oils are the most culpable, crisp and savoury foods the least. It appears more easily after repletion. The things which engender appetite combat it; those which destroy appetite encourage it. Anorexia and nausea are very close allies. Now certain emotions, oils and fats—as can be shown experimentally—all have the property of inhibiting gastric tonus, peristalsis, and secretion. An oily or creamy test-meal, as I have proved in my own person [1], takes twice as long to leave the stomach as a gruel test-meal and evokes a much slighter acid response. Similar effects were produced by the suggestion of nausea under hypnosis by Bennett and Venables [2]. Appetite and hunger and well-being on the other hand are associated with activated tonus, peristalsis, and secretory activity. In practice we meet with nausea in chronic gastritis, in which the normal responses of the stomach are inhibited by the thick layers of mucus which coat its membranes; in jaundice and cholecystitis, conditions in which fatty foods are badly tolerated; and in anaemic states, in which appetite is diminished when the stomach, like the heart, sharing the general anaemia, suffers loss of its usual functional efficiency. In the presence of acute peripheral pain and emotional states, in faintness and vertigo, the stomach expresses with nausea the general consequences illustrated in the case of the vasomotor system by pallor and shock-like phenomena. In each case the tone of plain muscle is inhibited.

Nausea is absent conversely in those painful gastric disturbances like duodenal ulcer, in which tonic and peristaltic

activity are exaggerated. One of the most interesting demonstrations of the behaviour of the stomach during nausea is given by screening after a barium meal during an attack of migraine. The stomach is then seen to be inert, the barium lying as in a bag, with little or no peristalsis and prolonged delay in emptying. Barclay [3] has observed a drop of 3 inches in the lower border of the stomach just before fainting occurred and has recorded the same event in the case of a patient who was given nauseous substances to smell.

From parallel clinical, physiological, pathological, and radiological observations such as these we conclude that the gastric, and that is perhaps the major, part of nausea is associated with a depression or inhibition of the normal tonic and peristaltic functions of the stomach. When confronted with nausea in practice it is particularly important to discover whether it occurs in concert with headache as in migraine and some cases of astigmatism, or with giddiness as in labyrinthine disease; whether it has a morning incidence as in pregnancy and gastritis; whether anaemia or anxiety be evident; or whether it comes in 'waves' and is associated with scapular pain and right subcostal pain as in cholecystitis. Its time relationships and symptomatic associations rather than the symptom itself are the helpful points in diagnosis. If we except the hypnotic experiment and Barclay's experiment with smells our information concerning nausea may be said to have been mainly deduced from physiological information and clinical observation. It is difficult to suggest at present how it might be more usefully studied experimentally.[1]

The Sense of Dying

We come lastly to that strange symptom usually referred to as the *sense of dying*, the *feeling of impending dissolution*, or *angor animi*. Until this has been experienced it would seem that we can have no conception of its character. With rare exceptions it is not present even on the threshold

[1] E. P. Poulton and W. W. Payne (*Journ. of Physiology*, 1923, lxv. 157) by personal experiments have demonstrated oesophageal relaxation in association with nausea.

of death. It has no kinship with pain or other familiar bodily discomfort. It differs from all ordinary forms of faintness. And yet it is more real and arresting and distressing to its victims than any of these. It is not mere anxiety or panic and, although it necessarily engenders apprehension, it is quite wrong to describe it as the *fear* of impending dissolution. I have known two courageous young men, dangerously occupied, who suffered from it. Clifford Allbutt insisted that it should be considered as 'an organic sensation' [4], and so, for many reasons, I believe it to be. According to my own notes it occurs in some 20 per cent. of cases of angina pectoris and distinctly less frequently in the status anginosus of coronary thrombosis than in the angina of effort. I have also recorded it in angina cruris—so-called intermittent claudication, and in a case of Raynaud's disease, in each of which it was synchronous with the vascular manifestations [5]. It occurs in 10 per cent. of cases of labyrinthine vertigo. It may accompany anaphylactic shock. Sir Arthur Hurst told me that he had noted it after injections of adrenalin. I find that it is present in no less than 60 per cent. of my cases of that peculiar syndrome described by Gowers as the *vaso-vagal attack*, and by German authors as *angina vasomotoria*. In most of the remaining 40 per cent. of cases kindred sensations as of 'fading away' or 'going under an anaesthetic' are mentioned. Finally it may occur in organic central nervous disease involving a precise and particular localization which seems to lend confirmation to the hypothesis I have advanced [5] in regard to the genesis of the symptom.

As my best opportunities of observing angor animi have been in cases of the vaso-vagal syndrome I shall here describe two characteristic cases:

CASE 1. *A woman of 62, who had previously been under my care* for general ill health and cholecystitis, became the victim of severe emotional stress and developed attacks of retrosternal pain with a sense of constriction in the chest and tingling in the left arm. In the attacks her husband described her as of 'the colour of a piece of marble'. Gradually the character of the attacks changed. The main symptom was now a sense of dying, out of the belief in which she could in no way be persuaded. With it she felt an extreme sense of

constriction of the chest and experienced a curious feeling between her left clavicle and her neck as though the head were being drawn down on that side. She also had *tingling in the fingers*. The attacks would last from half an hour to one hour, were not induced by effort, and she remained with a feeling of profound prostration for several days afterwards. In the attacks she was pale and cold. Her pulse-rate, normally 70, fell sometimes as low as 32 to the minute, and I myself counted it at 44 at the end of an attack. Brandy gave some relief; tabellae trinitrini little or none. Her blood-pressure varied remarkably from time to time between 130–80 and 180–90. In one very bad attack she lost consciousness and the pulse-rate fell to 19 to the minute. The respirations were rapid and shallow. Her husband, a medical man, was convinced that she was dying. She was made to inhale amyl nitrite when the pulse quickly rose to 52 and some colour returned. There was no clinical, electrocardiographic, or radiological evidence of arteriosclerosis or heart disease. Eventually removal from the causes of her emotional stress cured her of all the major attacks, although she still had an occasional return of praecordial discomfort and the strange feelings above the clavicle.

Case 2. A man of 57 had his first and only attack on board ship during a rough sea when for the first time in his life he suffered sea-sickness. In the lavatory he suddenly felt dreadfully ill, became still and rigid, was unable to speak, move, or draw in a deep breath, and was convinced that he was dying. In this condition he was found by chance and carried to the deck by a sailor. There, when he at last got his breath, he felt as if he had received a sudden blow at the back of his neck.

From these cases and many others we learn that the vaso-vagal syndrome may include the following symptoms: First and foremost the sense of dying, and after this prostration, coldness, immobility, constricted breathing, and tingling or a leaden feeling in the arms, and often pain or discomfort of anginal distribution. Objectively the patient is pale, the pulse is very slow or quickened, the respirations are shallow and rapid, and, probably as a result of this, minor tetany may be present. There are thus the same sense of constriction and immobility which accompany angina pectoris, together with disturbances of cardiac sensation. There are the same pallor and vasomotor disturbance which accompany shock, fainting, and vertigo. Prostration follows such as is seen in migrainous attacks. Unconsciousness occurs occasionally to remind us of epilepsy and fainting. There are remarkable variations in pulse-rate and blood-pressure.

All these events point to some profound nervous storm, and some of the phenomena, such as the bradycardia, inevitably suggest a vagal influence. There are ample reasons why Gowers should have included the syndrome in his classical monograph on *The Borderland of Epilepsy*. A case has recently been described in which a vaso-vagal attack was always followed later in the day by a true epileptic seizure [6].

Vaso-vagal attacks, in my experience, almost invariably occur in persons who are afflicted simultaneously by chronic or recurring mental distress and by some general cause of physical ill health, such as anaemia, digestive disorder, the menopause, or a chronic infection. In one case the attacks were repeatedly precipitated by the uncomfortable visceral stimulus of colonic irrigation, and I have notes of other cases in which disturbed function in one or other of the hollow viscera was associated with angor animi. Something similar in respect of the associated malaise and shock has also been induced in healthy men by arterial puncture [7]. In angina pectoris the angor may be synchronous with the pain and the sudden arrest of movement. This powerful triple reflex is Nature's 'pistol to the head'. 'Another step and you are a dead man' would seem to be its purport. It would seem that an emotional, a visceral, or a vascular stimulus may be the 'trigger' for angor animi, but that in the absence of general ill health and nervous instability of constitutional origin, or brought about by anxiety, it is unusual for the full vaso-vagal attack to follow.

Viewing the vaso-vagal syndrome as a variety of nervous storm, akin to epilepsy and migraine, and having particular regard for the vagal phenomena and the sinister leading symptom, it has seemed not unnatural to suggest that the medullary level, where the centres of life itself reside, might be involved in this storm. It is at this point that we must begin to look for proofs of the hypothesis. My colleague Sir Charles Symonds has told me of two interesting cases in which he has encountered the sense of dying in association with organic central nervous disease. One case was that of a child with signs of a tumour involving the medulla oblongata. The other was that of a man with central nervous

syphilis who was found at necropsy to have miliary gummata in the same situation. I have under my care at the moment a middle-aged man with tabes dorsalis and severe vaso-vagal seizures.

May we not venture to claim that our symptom, although still very imperfectly understood, has been tracked to its point of nervous origin? I believe we may.

The practical outcome of these considerations, apart from their contributions to diagnosis, is that, excepting in angina pectoris of organic origin or such a rare mischance as disease of the medulla itself, the alarming sense of dying has no grave prognostic significance. In vertigo and vaso-vagal attacks we may give the fullest reassurance and so find ourselves in a much better position to handle the situation wisely than we should do if perplexed by the distressing character of the patient's complaint and the disquieting objective manifestations of the attacks.

Conclusion

Let us briefly review the methods employed in the investigation of these three symptoms, for they may perhaps serve as a guide to the investigation of other subjective phenomena.

In the case of the particular pain of spastic colon the method was firstly to define the symptom itself by estimating its degree and discovering the special qualities peculiar to it, and then to review carefully its associations in the shape of other symptoms, physique, temperament, and objective findings.

In the case of nausea, a familiar symptom but one lacking the precision of pain, the method was to consider common experience, the physiological and pathological provocatives of the symptom, the various disorders in which it is prominent, and the factors common to these. Finally we obtained the help of certain objective studies of the stomach by X-rays during bouts of natural and induced nausea.

In the case of angor animi, or the sense of dying (a symptom which is quite beyond imagination and common experience, but one which is felt intensely and described with an

emphasis or horror giving it a reality as impressive as the reality of pain), the method was again to consider the known conditions in which it occurs, to record and correlate associated phenomena in each of these, to advance the hypothesis that the symptom could best be explained as being due to some disturbance involving the neighbourhood of the vagal nuclei, the realm that governs the functions of life itself, and then finally to discover that organic disease in that confined region is in fact capable of reproducing the symptom.

The methods, in brief, were those of observation, record, and analysis. The conclusions to which they lead us are as yet provisional and incomplete. It is not to be expected that the results of such methods will ever have the finality of successful experiment, but we are entitled to urge that they are scientific and serviceable. They are scientific because they constitute a systematic inquiry after truth. They are serviceable because they provide a useful exercise for the mind; because they carry us beyond ignorance and furnish us with reasonable hypotheses; and, most of all, because they improve diagnosis, prognosis, and treatment.

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VI

THE NATURE AND RELIEF OF SOME COMMON GASTRIC SYMPTOMS[1]

The science of symptomatology, whatever appeal it may make to our philosophy, is essentially a practical science. Its concern is with common things, for symptoms are always and everywhere available. If we analyse our diagnostic achievements we find, with the passage of time, that they depend more often upon a proper appreciation of subjective symptoms than upon any special skill or training in the methods of physical examination. To accurate history-taking and the study of personality full credit must be given, and the routine overhaul must never suffer neglect, but a detailed interrogation in respect of the patient's own sensations is the physician's surest tool.

In practice only a small proportion of our patients are found to present frank physical signs, and when they do so their disease is active or advanced. But no patient, unless it be for purposes of life insurance or a health certificate, comes to us without a symptom. It is true that we all learn to associate certain symptoms or groups of symptoms with certain diseases, disorders, histories, and temperaments, and so by degrees make better use of them. But we should not rest content with this knowledge; we should seek to discover the fuller physiological significance of each symptom, for then its value is doubled.

If physical signs may be called the morbid anatomy of bedside medicine, symptoms are its morbid physiology, and they usually precede the development of signs. This is well shown by any familiar symptom, such as angina pectoris, in the presence of which we are often entitled to surmise the presence of coronary arteriosclerosis long before the stethoscope or the electrocardiograph can demonstrate organic change. Each symptom expresses a perturbation of some normal function, an exaggeration or a depression of a

[1] *Guy's Hosp. Gazette*, 1934, xlviii. 463.

healthy vital reflex. The dyspnoea of exertion in health is physiologically allied to the dyspnoea of heart disease at rest. Many of the symptoms of disease, such as dyspnoea, dizziness, and nausea, can be reproduced by suitable over-actions or inhibitions artificially induced in healthy subjects.

In no group of diseases do we have to rely more upon symptoms than those collected under the general heading of the dyspepsias. The descriptions of their feelings which patients furnish may be vague or confusing at times, but this is partly our own fault, because we are not sufficiently at pains to develop a proper technique of interrogation.

The majority of the dyspepsias are due to errors of gastric or oesophageal function occurring independently of organic disease, but even in the presence of organic disease we are commonly, from the nature and small size of the lesion and the inaccessibility of the viscera, deprived of the advantages of objective evidence.

Before directing attention to the six symptoms which it is my purpose to review, let me remind you briefly of what is known of the normal sensibility of the stomach. Appetite, hunger, satiety, and repletion are all normal sensations, and in part, at least, appreciated by the stomach itself. To the best of our belief the mucosa and peritoneal coats of the stomach are almost or quite insensitive to all those tactile, thermal, chemical, and painful stimuli which the skin and the mucosa of the mouth so readily appreciate. The muscular coat, however, is appreciative of alterations in tonic or peristaltic activity and states of 'stretch', and Carlson clearly demonstrated that the hunger sensation is accompanied by and synchronizes with increased peristalsis. With exaggerated degrees of muscle-tension pain occurs.

I propose to consider in turn hunger-pain, flatulence, heartburn, acid regurgitation, water-brash, and hiccups. The first and the third of these are wholly sensory phenomena. In the remainder there are sensory discomforts with objective associations. In the last-named only are the attendant discomforts remote from the upper alimentary tract, although this is commonly, if not invariably, their seat of origin.

In each case I shall discuss the nature of the symptom, its common morbid associations, what we know or can at present infer in respect of its physiology, and, lastly, its treatment.

Hunger-pain

Hunger-pain is felt in the epigastrium. It is usually described as 'gnawing' in character or as a 'bad ache', and it is frequently associated with a sensation of sinking, hollowness, or emptiness. It is fairly strictly localized, but occasionally an attendant discomfort spreads upwards into the chest. It develops characteristically between two and three hours after the last meal, and endures for an hour or so unless relieved by food, fluid, or alkaline medicines. Cold, fatigue, mental worry, and tobacco tend to increase it; warmth, peace of mind, and holidays relieve. It may be associated with water-brash and vomiting and with sensations of gastric flatulence.

It is most frequently encountered in cases of duodenal ulcer, but occurs with some gastric ulcers, and occasionally with early growths of the stomach. It is also, however, registered in some cases of dyspepsia due to gall-bladder and appendicular disease, and, at times of stress or in association with tobacco-excess in patients endowed with the over-active, over-acid stomach which we recognize as contributory to the ulcer-diathesis, it may arise without a lesion of any kind. The fact that it may occur in the absence of any gastric or duodenal lesion is the best evidence that it does not express these lesions, but only the nervous perturbation of function which they are liable—as foci of irritation—to engender.

Whether the irritation be local, distal, or central, we believe its effect to be the production of a hypertonic 'behaviour' or 'posture'—that is to say, an excessive tonic and peristaltic activity—in the pars pylorica shortly before the stomach is due to empty. This abnormal increase in muscle tension is the cause of the pain. When food or fluid is introduced into the normal stomach the normal response is a relaxation of tension to accommodate the increased

content. If this did not occur, intragastric pressure would rise continually during a meal. The occurrence of this same relaxation in disease eases the pain, which alternatively departs eventually when the stomach empties completely. Alkalis, such as bicarbonate of soda, are believed to relax the cardiac and pyloric sphincters and so ease the situation by an expulsion of gas and a diminution of intragastric pressure. At one time hunger-pain was regarded as a symptom of hyperchlorhydria, but I have seen it in association with achlorhydria, and many people with hyperchlorhydria never experience it.

The treatment of hunger-pain includes the treatment of the underlying cause, but suitably frequent feeds and alkalis play an important part in all those conditions in which the cause cannot be eradicated, and also play their part in promoting healing of ulcers by giving rest to the diseased part.

Flatulence

In questioning patients about flatulence we should always determine first of all whether they mean stomach-wind or bowel-wind. I am here only concerned with the former. The symptom is characterized on the one hand by sensations of fullness or discomfort of varying degree in the epigastrium or chest, and on the other by eructations of gas or belching. The eructated gas is usually odourless, but in certain conditions it may be foul. When the smell is of 'rotten eggs' or *sulphuretted hydrogen*, *gastric stasis* with protein decomposition is always present, and the *symptom* is *therefore* of *real diagnostic value* in *pyloric* stenosis or obstruction. Very occasionally it is noted as a *transitory symptom* in association with an infective gastritis. Eructations of flatus or bowel-wind are pathognomonic of gastro-colic fistula, and make the diagnosis even in the absence of radiological proof.

Odourless flatulence is one of the commonest symptoms of daily practice. It may be due to trivial functional disturbances or serious organic disease. The sensations of flatulence may clearly be produced by an actual excess of air or gas in a normal stomach or by a normal content in

a hypertonic organ. There is no good evidence that gas can be evolved in or diffused into the stomach sufficiently rapidly, lacking an obstructive lesion, to cause discomfort or repeated eructations. Repeated and noisy eructations are always due to air-swallowing, and even the flatulent discomforts of organic disease are commonly aggravated by this subconscious habit.

Of organic lesions in which flatulence is a common complaint I have already mentioned duodenal ulcer. In gall-stones and cholecystitis it is a more pronounced feature, and 'bursting flatulence' is a frequent complaint in the dyspepsias of gall-bladder disease. Eructation also commonly terminates anginal attacks and, because of this, anginal pains have often been erroneously nttributed to dyspepsia.

The habit of air-swallowing, or aerophagy, is initiated by forcible attempts to relieve a gastric discomfort by eructation, the act being preceded by gulping of air. This gulping, which can be seen and heard by any observant witness, becomes established as a conditioned reflex and may cause years of misery. Air-swallowing is sometimes initiated by the repeated swallowing of mucus necessitated by pharyngeal catarrh, and occasionally as an aftermath of ether-anaesthesia. A simple explanation and instructions to avoid forcible eructation may result in dramatic cures where other treatments and endless prescriptions have failed, as they must fail in that they take no recognition of the cause of the symptom. Peppermint drops or bicarbonate of soda in hot water help to alleviate transitory post-operative flatulence and the flatulence due to the disturbed gastric motility of organic disease, but even in these cases suitable explanation plays its part.

Heartburn

Heartburn, one of the commonest, has also been one of the most elusive, of dyspeptic symptoms. It has also suffered confusion with water-brash and acid eructations—two entirely distinct symptoms. The sensation is characteristically one of burning in the course of the gullet. Its distribution

is vertically linear, and it may be experienced at any level between the pomum Adami and the xiphisternum. It changes its level and fluctuates in intensity, and may endure for minutes or much longer periods. It is not, as a rule, accompanied by eructations of fluid. It may be, but is not necessarily, eased by food or alkalis. It is not a symptom of organic disease, but is an association of hurry and worry, of carbohydrate excesses, of anaemic dyspepsias, and (replacing the nausea of the earlier phase) it is, with many women, a most troublesome symptom in the later months of pregnancy.

At one time heartburn was thought to be a symptom of 'acidity', largely because alkalis may relieve it, but it can occur in patients with complete achlorhydria, and it is not a particular feature of dyspepsias associated with hyperchlorhydria.

By analogy with other burning pains, such as tenesmus, we may argue that it is due to some degree of tonic oesophageal contraction, and the experimental work of W. W. Payne and E. P. Poulton[1] supports this hypothesis. Sodium bicarbonate and alokol—a proprietary preparation of aluminium hydroxide—probably by relaxing the cardia, give the best help, but dietetic adjustments and improvements in general and nervous health also play their part.

Acid Regurgitation

This symptom describes itself, and is characterized by a sudden regurgitation into the gullet and mouth of sour fluid, which may even roughen the teeth. It is the only direct symptom of gastric hyperacidity, and, even so, occurs only in a limited proportion of patients with hyperchlorydria. The treatment is the treatment of any underlying cause, such as duodenal ulcer, tobacco excess, or rushed irregular meals, combined with alkaline therapy.

Water-brash

By water-brash we imply the sudden arrival in the mouth and gullet of large quantities of clear, tasteless, watery

[1] *Quarterly Journ. Med.*, 1923, xvii. 53.

secretion. It is to be distinguished from the excessive and stringy mucoid secretion of alcoholic oesophagitis and some oesophageal obstructions. It occurs more frequently in duodenal ulcer than any other dyspeptic disease, and may, perhaps, be regarded as an exaggeration of the 'mouth-watering' which is proverbially associated with hunger, but better manifest in dogs than men. It is synchronous with the 'hunger-pain', is due to a sudden secretion of saliva, and possibly has a protective purpose, for, if swallowed, it may even relieve the pain. Pain in the parotids sometimes accompanies this sudden salivary hypersecretion.

Hiccups

Hiccups are usually due to trivial causes and regarded as a domestic joke. When, however, they occur in old people and are long continued they may cause serious exhaustion and the gravest anxiety. They may also be of evil import as accompaniments of acute abdominal catastrophes and uraemia. In children they are particularly frequent and innocent, and probably to be related to bolting of food and starch-excess. Some people are unable to take very hot or peppery soup without immediate hiccups. They are a familiar manifestation of an alcoholic bout. In all of these it must be assumed that the symptom is a reflex consequence of gastric irritation. Its mechanism would seem to include a sudden closure of the glottis in inspiration, with a simultaneous 'twitch', or arrest in its descent, of the diaphragm. In the abdominal catastrophes the stomach is usually dilated, and filled with turbid brownish fluid and sometimes regurgitated intestinal contents. In uraemia, either uraemic gastritis or a nervous intoxication might be invoked. There are also occasional epidemics of hiccups, and one followed or accompanied the wave of encephalitis lethargica shortly after the First World War, although there was no final proof that it was due to the same cause.

In their graver forms hiccups are most intractable. Gastric lavage in cases of dilated stomach may put a stop to them. In the unexplained and long-continued hiccups of old people, and occurring at any age in the

epidemic variety, it is customary to try oil of cajuput or tincture of iodine by the mouth, but they are usually ineffectual. An ice-cold application to the epigastrium sometimes succeeds. The induction of violent sneezing (not applicable in abdominal cases or the presence of exhaustion) is a remedy as old as the Socratic Dialogues, and is sometimes most effective. Stronger remedies may, however, be necessary, not excluding heroin and morphine, and even with these the spasms may continue during sleep.

Conclusion

What do we gain from a fuller understanding of these familiar symptoms? First of all we gain a better precision in diagnosis and improve our aptitude for early diagnosis. Our dependence upon objective measures and the accessory aids of the X-ray department and the laboratory is diminished. The stories of our patients develop a meaning which they previously lacked, and a practical morbid physiology, even though it stand in need of other proofs, adds interest to our handling of disorders which have the reputation of being rather dull or difficult. Finally we come to rely more upon simple explanations and reasoned régimes and less upon the eternal bottle of bismuth and soda, which, valuable though it be in some conditions, has no right to be regarded as a panacea for all digestive ills.

A similar attention to detail in considering the symptoms of cardiovascular, respiratory, and other diseases is similarly rewarded. Let us therefore endeavour to remain constantly curious about the nature and meaning of every symptom which our patients bring to us.

VII

THE NATURAL HISTORY OF DUODENAL ULCER[1]

THE subject of this lecture is one which has engaged the thoughts of physicians and surgeons for a quarter of a century, but which still supplies them with unsettled problems. Mindful of the title of this office and of my inability to expound the anatomical or the surgical precepts of John Hunter, I have felt that I might at least, in humble fashion, demonstrate my devotion to the observational method of John Hunter the *naturalist*. The physician *is* or should be, above all, a student of the natural *origins*, associations, and sequences of disease, and in this capacity he can best render his contribution to prognosis and to therapeutic principle.

During the past twelve years I have had considerable opportunities of studying the problems of duodenal ulcer both at hospital and in the course of private practice. My close association with Sir Arthur Hurst and his thorough methods of inquiry has furnished a constant stimulus, and I have been indebted to my friends, the surgeons and the radiologists, for much instruction. Increasing familiarity with the disease has bred anything but contempt. Each year there have been new observations to record and new explanations to seek. The vast fund of information in the literature and the steady output of special researches on the subject notwithstanding, a broad review of the natural history of ulcus duodeni is, I believe, justified by the following four considerations:

1. *Duodenal ulcer is a prevalent disease, and there is evidence (although due allowance must be made for growth and concentration of population and for improvements in diagnosis) that this prevalence waxes rather than wanes under the existing conditions of civilized life.*

An inquiry into the admission-rates of some common diseases at Guy's Hospital shows that, on the average, 100

[1] Hunterian Lecture delivered before the Royal College of Surgeons, 5 February 1932 (*The Lancet*, 1932, i. 327).

cases of duodenal ulcer are admitted annually—that is to say, about 1 per cent. of all admissions—a figure somewhat less than the admission-rate for tuberculosis (all forms) but greater than that for all the pleurisies and lobar pneumonias combined. In addition, large numbers of cases are treated in the Out-Patient department. In my private practice, which has a general character—albeit with an abdominal bias—the ten most frequent diagnoses are duodenal ulcer, anxiety state, constipation, cholecystitis and gall-stones, hyperpiesia (with its cardiac and neurological sequels), tuberculosis, anaemia (all forms), migraine, spastic colon, and obesity. Of these, duodenal ulcer heads the list, accounting for approximately 5 per cent. of all my cases.

Wilkie [1], stressing the steady increase in the cases of perforation at the Royal Infirmary, Edinburgh, in spite of improvements in diagnosis and treatment and a multiplication of the smaller hospitals capable of dealing with these catastrophes, reasonably argues that the total incidence of the disease is rising. At Guy's Hospital the same thing is to be observed. Dividing the period 1910–29 into four five-year periods the admission-rates for perforated duodenal ulcer were as follows:

1910–14	48 cases
1915–19 (war period)	20 „
1920–4	87 „
1925–9	115 „

A part of this increase may be due to the fact that surgeons have come to observe a better precision in locating ulcers with reference to the pyloric sphincter. The annual total of deaths from duodenal ulcer in England and Wales has almost doubled in the last decade (see below). It seems doubtful whether this increase can be wholly accounted for by such factors as growth of population, improved recognition, and better habits of precision in recording the site of the ulcer. Moreover, the deaths from gastric ulcer have shown a contemporary and parallel rise. In both cases the increase is much more conspicuous in the males.

2. *Although the mortality of its most serious complication has been remarkably diminished by surgery, duodenal*

ulcer continues to take its toll and remains, through painful dyspepsia and occasional haemorrhage, a serious cause of disability and lost efficiency among members and classes of the community often endowed with energy and usefulness above the average and sometimes with outstanding ability.

3. *Although of all the dyspeptic disorders duodenal ulcer presents the most clear-cut clinical picture, its leading characters and natural behaviour are not so widely appreciated in the profession as they might be.*

Thus the length of time elapsing between first appearance of symptoms and diagnosis is usually to be reckoned in years rather than months. As the prospects of sound healing with a medical régime are best in the early days and diminish with the passage of time (*vide* Nielsen [2], whose figures support the common experience of physicians), the prompt recognition of symptoms is an essential contribution to therapeutics. Except in the case of doctors or medical students, I rarely see a case with a history of only weeks or months. Among 184 cases of duodenal ulcer referred to me in which the length of history is recorded, there were only 52 in which this was two years or less. I have notes of 48 cases with histories of 10 years and upwards, and of these 17 gave histories of 20 years or more, and a further 5 had had symptoms for at least 30 years. Among 121 cases (excluding cases of pyloric stenosis) in which the length of time between first symptoms and diagnosis could be roughly computed (all cases diagnosed in less than one year being counted as 'immediate') *the average interval was seven years.*

4. *Duodenal ulcer has supplied us with a number of problems in aetiology, prognosis, and treatment which are at present only partially solved.*

Doubts and difficulties continue to confront us. The wavering from medical to surgical and back to medical opinion, and the continued invention of new treatments and operations, are eloquent of our uncertainty. Extravagant claims have been made from time to time by protagonists of both the medical and surgical schools. Bacteriology, biochemistry, minute anatomy, and statistical inquiry have,

severally and collectively, failed to give the whole answe to our question. We have reached a *point* at which thera peutic experiment and specialized studies seem no mor competent to give help in practice than a general survey o the native disease as it occurs and as it varies in living man

To achieve such a survey with any completeness an within the compass of a single lecture would be an *impos* sible task. I must therefore content myself with a condensa tion of experience and must ask to be excused lengthy refer ences to the literature. All that is best of our knowledge o the subject is to be found in Moynihan's *Duodenal Ulcer* and in *Gastric and Duodenal Ulcer* by Hurst and Stewart. To the authors of these classics we must always remain in debted. If my remarks provide some small stimulus to the further pursuit of the old observational method (and with out the co-operation of this method experimental medicine can make but a halting advance), and if, in addition, I can adduce reasons for the adoption of a more judicial attitude in arranging the treatment of cases, I shall be well satisfied.

I have among my files the notes of upwards of 350 cases interrogated and examined by myself to which the diagnosis of duodenal ulcer is attached. From these I have separated for analysis only those in which the clinical story was con firmed by operation, haemorrhage (generally melaena), or a reliable radiologist. This series comprises (*a*) 218 cases, of which 24 had proceeded to the development of pyloric stenosis. To these I have added (*b*) 35 cases of anastomotic ulcer, and (*c*) 8 cases of other surgical disappointments fol lowing gastro-jejunostomy undertaken for the relief of a duodenal ulcer. My mental images are naturally coloured by an equivalent experience of hospital patients drawn from other sections of the community, but I have preferred to employ the material immediately to my hand and upon which all observations were intimate and personal.

The Origins of Duodenal Ulcer

Constitution

Wherein should we seek the beginnings of a disease which tends strongly to relapse or chronicity and which has no

basis in contagion or epidemic causes? Clearly, I think, in the peculiarities and antecedents of its victims or in their habits and environment. Preoccupied with the lesion and with hypotheses as to its mode of initiation and perpetuation by local bacterial and chemical action we have too long delayed our study of the soil in which it thrives. We have but to observe in sufficient number our patients as they come before us to appreciate that we are here confronted with distinctive human types or constitutions. Within these constitutions we may already discern certain physical, biochemical and psychological variants which between them supply what we may call the 'ulcer diathesis'. Thus, if our notes are sufficiently descriptive, we find again and again that our patients are delineated as 'lean and nervous' men, often tense and muscular and with brisk mental and physical reactions, or, alternatively, as robust and energetic and, when free from symptoms, of strikingly healthy appearance. There are even physiognomical characters which may impel us to hazard the diagnosis before the history is taken, but, as the disease itself may put a stamp upon the features, we cannot here be sure that we are concerned with heritable variations. The epigastric angle is commonly wide, and the observations of Faber [3] have enabled us to correlate this feature with the short, high, 'steerhorn' stomach of the radiologist. Moody, Van Nuys, and Chamberlain [4] find this type of stomach more common in the male sex. Campbell and Conybeare [5] have also associated this type of stomach with broad, athletic men on the one hand and with hyperchlorhydria on the other. Izod Bennett [6] and I earlier reported hyperchlorhydric curves in 8 per cent. of healthy male students. Psychologically these folk are energetic, restless, conscientious, intent on their projects, and not seldom given to anxiety of mind. If engaged in business their city lunch is an occasion not for respite and digestion, but for more business. Recognition of these facts is essential to a proper understanding of the disease, and to the handling of cases. No disease, however, should be summarily ascribed in any part to constitutional causes unless we can also demonstrate that it exhibits a familial tendency.

Other chronic maladies like gout, asthma, and epilepsy have long been accepted as having some basis in constitutional causes and provide positive family histories in approximately 25 per cent. of cases. Occasional reports on the familial tendency of ulcer had appeared previously, but it was not until 1921 that Hurst [7, 8], who is so largely responsible for our reawakened interest in the constitutional factor, laid emphasis upon the real importance of inheritance in this disease. In his paper bearing on the subject he quoted among others three family histories which had then come to my notice, including one in which three brothers were operated on for duodenal ulcer and a sister for gastric ulcer. In my present series (*a*) there were 23 instances (10 per cent.) in which a near relative—i.e. parent, child, brother, sister, aunt, uncle, or first cousin—was recorded as having had a duodenal ulcer. In one instance the father of the patient, two uncles, and one cousin, and in another a sister and two maternal cousins had been afflicted. Histories of 'dyspepsia' in near relatives are also common. If allowance be made for the infrequent recognition of duodenal ulcer as a cause of dyspepsia in the last and preceding generations, the frequency with which the diagnosis is missed at the present day, the customary inattention to the family history of a disease until its importance becomes widely accepted, and the difficulty always experienced in collecting and recording medical pedigrees, it seems probable that the actual incidence of positive family histories in duodenal ulcer would prove to be higher than these figures indicate.[1]

Sex, Age, and Occupation

Sex.—The well-recognized preponderance of male over female cases (four to one in the present series) must also have some bearing on aetiology. The broad epigastric angle and steerhorn stomach are commoner in the male sex. The

[1] Since this lecture was penned I have encountered yet another 'ulcer family', illustrating the sad consequences of an intermarriage between predisposed stocks:—Father D.U.; Mother G.U.; three sons D.U.; one daughter 'ulcer symptoms'; her son perforated D.U. and her daughter peptic ulcer. One paternal cousin in the middle generation D.U.

male of the type described spends his energies freely, often bolts or misses meals, often smokes excessively, and generally lacks the aptitude or opportunity for mental quietude in his life which falls more frequently to the lot of woman-kind.

Age.—The age-incidence of the disease is also instructive. Roughly half the cases are between the ages of 30 and 50, that is to say, within the period of life when work and worry most predominate. Duodenal ulcer is rare in childhood and, in fact, until after puberty, although occasional boyhood cases are to be found in any long series. It is rare for symptoms to make their first appearance after the sixth decade, although recurrences then and even into the seventies and eighties are not infrequent. The average age in my series at the time of consultation (excluding cases of pyloric stenosis) was 47 years. The youngest patient was aged 19, the oldest 83. The youngest calculated age of onset was 9 years, and there were others as young as 12 and 15. Positive family histories, as we should anticipate, appear to be more frequent in the youthful group.

Occupation.—The influence of occupation is hard to assess. No figures, for instance, are available for comparing the incidence of the disease in urban and agricultural communities. On a retrospect of experience it is difficult to avoid the conclusion that the life and occupations of the city are more productive of the disease. Among 94 cases in which the profession is recorded I find 28 doctors, 22 business men and lawyers, 13 officers of the Army, Navy, and Air Force, 7 dentists, and 24 in other walks of professional life. Doctors and members of the fighting forces also appear to show a special liability according to Hurst's figures from New Lodge Clinic [8]. The missed and bolted meals, and the cares which come to interrupt the smooth course of his digestion, might well be advanced in part explanation of the medical man's apparent predisposition to the disease. Its occurrence in the Services is merely a reminder that the disease is one of robust or active rather than frail or indolent constitutions. Lord Moynihan [9] has recently referred to his experience of cases in athletes of the first rank.

Other Aetiological Factors

Tobacco.—Smoking had been indulged in by the men almost invariably and sometimes in great excess, but although medical and surgical opinion unite in opposing the free use of tobacco by ulcer victims, and many patients appreciate that they are better without it, or even that it may aggravate symptoms, it is difficult to obtain concise proofs with regard to the part which this habit plays in determining the arrival or perpetuation of symptoms or the different incidence of duodenal ulcer in the two sexes.

Focal Sepsis.—Although it is a reasonable part of treatment to eradicate focal sepsis, and although the teeth or the appendix can often be shown to be unhealthy, the actual contribution of cryptic infections is still difficult to assess. Dental, tonsillar, and sinus infections are not necessarily followed by duodenal ulceration, even in persons predisposed by constitution or habits of life. Furthermore, duodenal ulcer may develop in patients in whom no focus can be found or who have long since been deprived of their teeth or vermiform appendix.

Environment.—I have referred to the possibility of a higher incidence of duodenal ulcer under the conditions of life in cities. With others I have also been struck by the promptly beneficent influence of a healthy out-of-door life on the active symptoms of the disease. A country holiday will frequently cut short an attack. Nervous influences play their part, for pain may cease on the first day of the holiday. One patient of mine could spend weeks ski-ing in the Austrian Alps, living on black bread and beer, without symptoms, but would relapse in his English home where his diet was carefully arranged. But more impressive than such isolated cases has been the story, repeated to me on several occasions, that men with duodenal ulcer, who were dyspeptics before their military service and again on their return to office life, were entirely free from symptoms under the hard physical conditions of active service abroad during the war.

Climate may also play some part. I have had patients who were free from symptoms in India but afflicted when

at home, and Col. E. B. Marsh, A.M.S., who made a particular study of duodenal ulcer among the troops at Aldershot, where he found it prevalent, later wrote to me from India to report that in twenty-two months in the East among British troops, differing only in that they were slightly older than the home troops, he had not seen a single proven case of ulcer.

Season, as Moynihan [10] showed long since, undoubtedly influences the fluctuations of the disease in the individual, winter, or autumn and spring recurrences being commonly described. Recurrences at these seasons or 'in cold weather' were specifically entered in my notes in 25 cases (12 per cent. of the duodenal ulcer series (*a*)). Raw east winds are particularly obnoxious to sufferers from duodenal ulcer. Seasonal infections may be a factor, but the majority of patients do not remark on this association.

Mental States.—A restless stomach accompanies a restless mind. In many cases anxiety and mental conflict seem to play a part in the aggravation of symptoms. In a minority of cases (although it be beyond proof) it is tempting to wonder whether the disease would have developed in the absence of psychological turmoil.

Aetiological studies are thus shown to be of some importance, and if we can cast our vision forwards to a time in which we shall be more concerned with the prevention than with the cure of chronic diseases of this class, it is clear that our method will find its basis quite as much in intimate studies of constitution, habits of life, occupation, and environment as in the refinements of chemistry, bacteriology, and animal experiment. In our choice of treatment of the active disease we must also remain attentive to these elements in its natural history, remembering that the success of therapeutic experiment in the long run depends even more upon knowledge and judgement than upon technique.

The Course of Duodenal Ulcer

I have referred to the long interval which commonly elapses between first symptoms and diagnosis. The chief reason for this is to be found in the natural tendency to

spontaneous remissions of symptoms. Patients and doctors alike in the first attack, delighted by the quick response to dietary care or 'a bottle of bismuth', with disappearance of all pain within a period of two or three weeks or less, are lulled into an attitude of false security and deem the 'bout of indigestion' past and done with. As Moynihan and others have clearly proclaimed, this behaviour is characteristic of the disease. If we are to judge by the early clinical course of duodenal ulcer (for symptoms surely bear some relationship to 'activity') there must be repeated attempts at natural healing, and this is a particular justification for medical measures at this stage. That spontaneous healing occurs is evident from the scars found in the course of routine post-mortem work. The first attacks may last no more than ten days and rarely more than three or four weeks, and they may be followed by free intervals of enjoyable health, with ability to eat all foods, enduring for six months or longer. The man who starts his illness with a melaena is really a lucky man, for by this means his diagnosis is declared and early and strict treatment instituted. Many patients go free all the summer months and suffer relapses between October and March. With the passage of years the bouts of dyspepsia become more prolonged and frequent. And so the disease may drag on intermittently for five, ten, or even twenty years, with or without distinctive complications and often, in the latter event, without a diagnosis.

Haemorrhage occurred at one stage or another in rather less than 40 per cent. of this series (*a*), but it should be recalled that many cases unconfirmed by operation, X-rays, or haemorrhage were excluded, so that the figure is clearly too high. Most authors of experience record haemorrhage as occurring in approximately 25 per cent. of cases. *Allowing for the many 'missed' dyspeptic cases, all recorded per*centage figures for the complications must be accepted as too liberal. Perforation (including 'local perforations') occurred in 10 cases of the duodenal ulcer series (*a*), and in the anastomotic ulcer series (*b*) (*35 cases*) *in 7 cases before* and 3 after operation. These figures give no indication of actual frequency of perforation. The physician is rarely

called to these emergencies. It is, however, a much rarer complication than haemorrhage. Pyloric stenosis occurred in 24 (11 per cent.) of my cases, series (*a*). The serious complication of involvement of the head of the pancreas, with its particular syndrome (to be described later), occurred in 2 per cent. of this series.

Mortality of Duodenal Ulcer

It is impossible to estimate the death-rate of a disease so widespread and yet so ill recorded as duodenal ulcer. Even allowing that the majority of deaths among patients of the hospital class occur in hospital, we can obtain no accurate measure, for hospitals not only attract the cases of perforation and haemorrhage in undue proportion, but also admit only the more serious of the dyspeptic cases. In twenty years at Guy's Hospital there have been 153 deaths among cases of duodenal ulcer. Of these, 70 followed perforation, 25 followed haemorrhage, and the remainder were indexed as due to various secondary complications of perforation or of operation undertaken for the relief of the disease or of its complications, or to intercurrent disease. That is to say, in a hospital admitting about 100 cases a year, about 7 or 8 cases a year die from all causes. For every one of these 100 cases admitted to the wards there must be several others from the same communities treated as out-patients and in their homes, or remaining undiagnosed and untreated. In general, although its interruptions to health are numerous, the menace to life of a duodenal ulcer is not a very grave one. According to the Registrar-General's returns there were 1,140 deaths (male) and 160 deaths (female) from duodenal ulcer in England and Wales during 1930, as compared with 552 (male) and 129 (female) in 1920. These figures are sufficiently arresting, and yet they must represent but a small percentage of the total army of recognized and unrecognized cases.

The Symptoms of Duodenal Ulcer

Moynihan [10] has rightly insisted on the anamnesis as the main plank in the diagnosis of duodenal ulcer. This

should include nll proper inquiries into personal and family history, environment, occupation, and habits, for these may serve not only to complete the opinion, but also to balance judgement in therapeutic decisions. But above all our interrogations must deal intimately with subjective phenomena. In the majority of cases it should be possible to arrive at a diagnosis of duodenal ulcer from the history and symptoms alone, and before the physical examination or accessory measures, such as radiology and the test-meal, have been called upon to play their part.

The leading symptom is the pain. It is true that an ulcer may be present to the tune of 'wind' or 'acid vomiting' and that the patient may deny the occurrence of true pain, but this is not usual. Employing a method of pain-analysis which I have previously described we may consider the pain of duodenal ulcer under ten headings, having reference to (1) character; (2) severity; (3) situation; (4) localization (or extent of diffusion); (5) paths of reference; (6) duration; (7) frequency; (8) special times of arrival; (9) and (10) aggravating and relieving factors. The character of the pain is described with great consistency as 'gnawing' or, alternatively, as 'aching' or 'like a toothache'. There is no intermission, although there may be slight fluctuations while it lasts. It is 'wearing' and 'worrying' but not so severe, as a rule, as to prohibit work, although it may hamper efficiency and concentration. With the occasional complication of pancreatic erosion it may, however, become very severe and even require morphine for its relief. Its situation is indicated by the patient with the finger-tips in mid-epigastrium or slightly to the right in more chronic cases; it is then generally at a lower level than that indicated by the right subcostal gesture of cholecystitis. It has a precise position and localization, but in severe, old-standing cases, and especially when flatulence with aerophagy is pronounced, it may 'spread' widely into the chest. When the pancreas is involved it 'goes through' to the back at the same level and, occupying the region of the twelfth rib (appreciably lower than the subscapular reference of gall-bladder disease), it may even create a suspicion of a right renal lesion. In these

cases, too, the anterior pain may be 'right subcostal' rather than 'epigastric'. The pnin is absent on waking, and remains in abeyance until some two to two and n half hours after breakfast. Arriving, let us say, at 11.30 a.m. it will persist for an hour or more until relieved by lunch, but it may return again before tea nnd again in the evening. Rearrangements of diet or meals will modify the behaviour of the pain. In cases of long standing a special time of occurrence is 2 a.m., when it wakes from sleep and lingers for an hour or two unless assuaged by food, a warm drink, or medicinc. It is aggravated by fasting, worry, fatigue, and cold, and sometimes by smoking. It is relieved by food, drink, warmth, rest, peace of mind, and alkalis. Dclayed pain, first noted in 1828 by Abererombie [11], and the hunger-pain with relief by food so clearly portrayed by Moynihan (although they nre occasionally due to other causes—i.e. gall-stones, appendicitis, gastric ulcer, worry, tobacco-excess, and very rarely carcinoma of tbe stomach) are thus the outstanding features of the disease.

We must not, however, neglect associnted symptoms. With or without the pain an epigastric 'sinking sensation', which probably represents an exaggeration of the normal gastric phenomena of hunger, is often mentioned. It is rare in other dyspepsias. Feelings of 'flatulence' or of fullness or a 'bursting sensation' may accompany or replace the pain. In nll cases of dyspepsin with pronounced flatulcnce the time of arrival of the symptom should be determined. If this is before meals and food gives ease, the possibility of duodenal ulcer (even in the absence of pain) must be seriously considered. The relief by eructation, and especially that which follows the use of bicarbonate of soda, suggests to the patient, nnd often to his doctor, that the case is 'merely one of flatulent dyspepsia', but flatulent dyspepsia must have n cause, nnd when the flatulence is rhythmical and at its worst before meals this cause is often duodenal ulcer. The gas eructated is odourless except in the presence of pyloric stenosis when it may have the taint of sulphuretted hydrogen. Vomiting has been regarded as a rare symptom in duodenal ulcer without stenosis, but this requires qualification.

Vomiting of food is, indeed, exceptionnl, but an acid wntery vomit is common especially with the more chronic ulcers. If later the quantity of this watery vomit increases or food is mingled with it, cicatricial stenosis should be suspected. Water-brash, or the sudden filling of the mouth with tasteless watery salivn, sometimes with necompanying pain in the parotid glands, is common and so chnracteristic of duodenal ulcer and so rare in other dyspepsias that it has genuine diagnostic value. One patient spontaneously and aptly described this symptom to me as 'a beautiful action of Nature'. Waking, he said, at night with bad pain he would shortly find his mouth filling with water as fast as he could swallow it; as he did so the pain steadily faded nway. Heartburn nnd nausea are not symptomatic of duodenal ulcer. Constipation, especially during the attacks, is a frequent complaint.

Apart from the local symptoms of the disease there nre certain general complaints which are very real to the patient nnd sufficiently rare in other gastric disorders to be of definitive value. I would particularly mention a feeling of physicnl weakness or exhaustion which is coincidental with the pain nnd nkin to feelings experienced in association with rectal spasm, excessive purgation, or other strong visceral crises. Mental irritability and loss of the power of concentration nre also described and are evidence of the powerful nervous influences nttendant on a visceral disturbance which carries with it, as well as pain, the psychic and physical phenomena of strong hunger. These symptoms also are relieved by food.

Factors which influence Severity, Character, Situation, or Food Relationships of the Pain

It should be mentioned, for it is not as widely appreciated as it might be, that the degrees of physical disturbance in duodenal ulcer show wide variations. The physician sees many cases in which the very mildness of the symptoms has led to a postponement of diagnosis. The surgeon, no doubt, sees a higher proportion in which pain is outstanding and severe. The severity of the pain tends to increase with the

chronicity of the ulcer. It increases at first with commencing stenosis, but later, as gastric dilatation supervenes upon hypertrophy, pain becomes less obtrusive and vomiting is the leading symptom. When the head of the pancreas is eroded by a posterior ulcer, the pain is at times unbearably severe and in the presence of this complication I have seen courageous men reduced to exhaustion and tears. Apart from haemorrhage it is the only symptom which the physician may be called upon to treat with morphine. It is worthy of note that haemorrhage may immediately abolish pain. When bleeding is severe, confinement to bed, morphine, and abstention from food, and later a strict dietary, clearly explain the relief, but even slight and at first unrecognized bleeding in an ambulatory case will have the same effect. In this circumstance a patient who has been suffering dyspeptic pains may actually hold himself better as regards his ulcer, and a failure to appreciate the significance of developing weakness and anaemia results. In the presence of early stenosis pain may become more 'grinding' or 'peristaltic' in quality. The situation of the pain commonly shifts to the right in the case of old-standing and adherent ulcers. The interval between food and pain diminishes in the early stages of pyloric stenosis and may be reduced to one or one and a half instead of the two or three hours previously experienced. It should also, however, be recognized that patients with extreme gastric 'hurry' occasionally show a very short food-pain interval. With ulceration involving the head of the pancreas all clear relationship to food tends to disappear and alkalis may cease to be effective.

Objective Signs

In the absence of pyloric stenosis with gastric dilatation or the rare discovery of a palpable inflammatory tumour it is too widely assumed that duodenal ulcer is a disease without physical signs. If carefully sought for, superficial, or more commonly deep cutaneous soreness, an increased abdominal reflex, muscular *guarding*, and *deep tenderness*—all confined to the right upper quadrant of the abdomen—will

be found either singly or in various combination in a high proportion of cases. These signs are more likely to be found with anterior ulcers, during stages of activity, and when pain is actually present. They disappear with healing. An increased reflex and muscular guarding are both more common than cutaneous hyperalgesia. Very occasionally a pilomotor reflex (goose-skin) confined to the same area may be observed when eliciting the abdominal reflex. The vasomotor consequences of active pain are sometimes manifest in the facies. Thus near relatives describe pallor or 'greyness' coincident with suffering in chronic cases. Phosphaturia is so common in association with active duodenal ulcer that I have come to expect a milky urine at the time of consultation in the majority of cases. How far it is related to the taking of alkalis or not I have been unable ta determine. Loss of weight is seldom conspicuous in uncomplicated cases.

Complications and Sequelae

Haemorrhage and perforation, cicatricial stenosis and anchorage of the ulcer-base to the head of the pancreas are the important complications. To these we must add the unsuccessful gastro-jejunostomy which, under modern conditions, has been a sufficiently frequent sequel to justify its inclusion in a study of the natural history of duodenal ulcer, and, in a retrospective way, may even help to illuminate the disease.

With the symptoms of haemorrhage and perforation I shall not especially concern myself, for they are well known. Haemorrhage, as stated, occurs in about one-quarter of the recognized cases. In many of my cases there was a history of two or more haemorrhages; 107 patients (series *a* and *b*) between them had 151 haemorrhages. Two patients, aged 76 and 56, died of gastric uraemia (alkalosis) with coincident haemorrhage, in 1 case following an operation. One, aged 56, died of coincident haemorrhage and cellulitis of the arm. One, aged 36, was transfused on account of a severe haemorrhage from a chronic ulcer, had an immediate reaction, and succumbed. Three cases, aged 76, 72, and 26, died of

The average duration of ulcer symptoms in 16 of my cases of pyloric stenosis was seventeen years. Only 2 cases gave histories of five years or less.

Involvement of the Pancreas

The duodenum is doubtless anchored to the pancreas by adhesions in many cases of posterior ulcer. In a small number the base of the ulcer may become more firmly welded to this organ or may actually erode it. In this event a clinical syndrome develops which is characterized by pain of unusual severity, not responding to strict medical treatment and alkalis, and even requiring morphine for its relief. The pain is commonly in the right upper quadrant and referred through to the right loin and may be chiefly felt posteriorly. Biliary and renal calculus are therefore sometimes wrongly diagnosed. Glycosuria occurs in some cases, and I have seen it come and go with the ulcer symptoms. The diagnosis is occasionally missed by expert radiologists in these cases, partly, I believe, because, with firm fixation of the duodenum, the prepyloric antrum is thrust over to the right during peristaltic activity, and so obscures the first part of the duodenum altogether. I have also seen cases in which a posterior adherent duodenal ulcer had escaped detection at operations undertaken for the relief of an ulcer or with a view to discovering the cause of pain.

A case of posterior duodenal ulcer involving the pancreas. Major A., a fine old soldier, aged 73, suffered for many years from periodic bouts

of dyspepsia with pain arriving some hours after food and relieved by it. Later the pain became greatly intensified and less clearly related to meals. He saw a surgeon who diagnosed gall-stones and, in spite of a negative cholecystography, operated for gall-stones. Finding no stones he drained the gall-bladder. During convalescence there was melaena on two occasions. The pain continued as before, and in his worst attacks, which took place at night, was sometimes so severe as to make him weep; it was accompanied by involuntary tremors and shivering. I saw him in pain and it was a pitiful spectacle. The pain was referred to the level of the eleventh and twelfth ribs on the right side posteriorly and there was guarding with tenderness over the right upper rectus. I diagnosed 'posterior duodenal ulcer involving the pancreas'. The radiologist reported 'appearances strongly indicative of an ulcer of the stomach about half-way between the cardia and the pylorus'. Mr. L. Bromley operated and found no gastric lesion but a posterior duodenal ulcer firmly welded to the head of the pancreas. A gastro-jejunostomy was performed and all symptoms were completely relieved.

Anastomotic Ulcer

For every 10 cases of duodenal ulcer referred to me I see one case of anastomotic ulcer. This gives no indication of the frequency of this sequel, for it is evident that surgical 'failures' find their way to the physician just as medical 'failures' find their way to the surgeon. The sequel, however, is a serious one and sufficiently common to justify careful inquiry into its causes and the greatest caution in the selection of cases for a gastro-jejunostomy.

The development of ulceration at or near the stoma has been variously attributed to faulty technique, unabsorbable sutures, the failure to eradicate focal sepsis, and neglect of appropriate after-care. My own experience suggests that more important than any of these are a faulty judgement in the selection of cases for operation and the presence of a strong constitutional predisposition. There was a positive family history in 7 out of my 35 cases of anastomotic ulcer (*b*), twice the rate of incidence in the duodenal ulcer series (a). The age at onset of the ulcer-symptoms for which the operation was undertaken was under 20 years in 6 cases and in 3 of these there was a positive family history. Early appearance of a chronic disease more usual in later decades should always suggest constitutional predisposition. I have

those of the original duodenal ulcer. There is hunger-pain with more or less relief by food. Both immediate and lasting relief of symptoms, however, even with the strictest medical care, is much less certainly attained than in the case of duodenal ulcer. Furthermore, pain and distress tend to be more severe and lasting. Haemorrhage may occur without premonitory pain. The most constant physical sign is a point of tenderness just above and to the left of the navel. Anastomotic ulcers are liable to the same leading complications as duodenal ulcer—namely, haemorrhage, perforation, and stenosis. The most wretched and often fatal complication is a gastro-jejuno-colic fistula of which the symptoms are pain, eructation of 'bowel-wind', or even vomiting of faeces, diarrhoea, anaemia, and emaciation. Fortunately it is rare. I have had two cases under my care in hospital and one in private practice. Hamilton Fairley and Kilner have recently reported on cases showing fatty diarrhoea with a megalocytic anaemia [12].

Other Complications of the Short Circuit

The most important remaining complication is 'vicious cycle vomiting', which is characterized by attacks of copious bilious vomiting at irregular intervals with or without pain. The 'dumping stoma', in which the common complaint is of a fullness and discomfort around and below the navel developing soon after meals and due to rapid over-filling of the small gut, is inconvenient but less crippling.

The Prospects of other Operations and Medical Treatment

It is too early to assess the later results of alternative operations such as gastro-duodenostomy, resection, and excision. Only after some twenty years are we learning to view in correct perspective the advantages and disadvantages of gastro-jejunostomy, and if we are wise we shall not too trustfully accept the promises made on behalf of the newer experiments. That they do not always succeed is already apparent. That they will often fail in the presence of strong constitutional predisposition or with injudicious selection of cases seems to me probable. Medical treatment

likelihood of perforation by increased intraduodenal pressure (as I have once successfully foretold) [18]. My policy is to oppose surgical treatment in youthful cases; in non-obstructive cases with short histories and adverse pedigrees or not previously accorded a strict medical treatment; in cases with recent haemorrhage, lacking other indications; and in cases in which X-ray and test-meal show gastric 'hurry', for here to accelerate emptying still further and to attempt an anastomosis in the presence of exaggerated motor and chemical unrest is to create just those conditions which may be held to favour secondary ulceration. Highly nervous individuals and elderly subjects should often be deemed unsuitable for surgery, even when the only alternative is continuous medical and dietary care. Economic and environmental factors must at times compel a modification of general policy. Surgical treatment should always be followed by a period of strict medical treatment and proper precautions thereafter. Psychological as well as physical requirements must be carefully studied.

All surgeons and physicians who undertake the treatment of this troublesome disease must endeavour to preserve the studious attitude, not lightly accepting opinion or submitting to the bias of their craft, and remembering always that they are not, in fact, concerned with duodenal ulcer the lesion, but with duodenal ulcer the disease, as it occurs and as it varies in individuals of special type and temper and differing daily circumstance. In each case, briefly, judgement must be based, not upon the presence of an ulcer, but upon a proper understanding of the whole patient and the whole disease.

As I have sought to show, duodenal ulcer has general effects on the body and the mind as well as general causes in them, and no effect or cause can be neglected.

In a restless and fretful age which has largely lost the old simplicities of diet and conduct, the most important contribution which we can make to the prophylaxis of duodenal ulcer is to furnish, as opportunity arises, sensible instructions to the community (and particularly to such families or individuals as manifest a constitutional or occupational

predisposition to the disease) with regard to the evils of missed and bolted meals, of excessive smoking, and of the prevalent habit of attempting to combine the process of digestion with anxiety and affairs. It is not extravagant to suppose that a cup of hot milk at 11 a.m. and bedtime would save many a harassed doctor or business man endowed with the diathesis from developing the disease.

The most important contribution which we can make to the therapeutics of duodenal ulcer is, by observing subjective symptoms, to ensure much earlier diagnosis, and, by observing the entire disease and the qualities of its victims, to achieve a wiser balance in our choice of method.

It is, I believe, a just criticism of surgery and medicine in the present era that they have concentrated on parts to the exclusion of the whole and on technique to the exclusion of philosophy. In duodenal ulcer no less than in many other maladies, we have come to rely upon too narrow a pathology. In our therapeutic quests we have been too little observant of physiological principle. We are all compelled by the magnitude of our subject to be something of specialists, but this should not necessitate an abandonment of that naturalistic outlook which marked the achievement of our old preceptors from Hippocrates to Hunter.

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VIII

ANOREXIA[1]

Few expressions of physical and mental well-being are more widely accepted and more generally appreciated than a good appetite. Conversely, few subjective symptoms, apart from actual pain, more promptly perturb the individual and attract the comment of his friends than failure of appetite. In trying to assess the progress of sick persons, the continued suppression or the return of the desire for food are indices upon which we place daily reliance. In our own personal experiences of ill health we recognize with each trivial febrile ailment that an abolition of our interest in meals constitutes a part of the malaise, and even in those lesser states of impaired fitness which we ascribe to periods of overwork or to some access of fatigues and worries, a diminished enjoyment of food is familiar.

We thus observe all gradations of anorexia, or 'the loss of the desire for food'. Its slightest forms are represented by those minor shades of disinclination just mentioned. At the opposite end of the scale is anorexia in its gravest degree occurring as a symptom of many chronic diseases and accompanying the active phases of acute fevers. In illness of intermediate severity every intermediate grade of anorexia may be encountered. It would therefore seem that appetite is an important and even a delicate physical response, and that we should have some understanding of its mechanism.

Appetite is so essentially a manifestation of normal bodily health that we should expect the physiologist to provide us with valuable information concerning it. I hope to show you that the clinical study of anorexia may also help to illuminate the problem for the physiologist.

What do we understand by appetite, and how far is it identical with or different from hunger? It is best characterized, I think, as a desire or readiness for food, and it is customarily regarded as a pleasant sensation. Hunger, on

[1] *Guy's Hosp. Gazette*, 1924, xxxviii. 305.

Pleasant tastes, pleasant aromas, a table well arranged, the dinner-bell, or the clink of spoons or glasses, and even the tactile sensory comforts of evening dress and clean napery, have all become inextricably associated with the idea of food, and singly or together are capable of promoting or enhancing appetite.

Cannon [3] says: 'Appetite is related to previous sensations of the taste and smell of food. Sensory associations, delightful or disgusting, determine the appetite for any edible substance, and either memory or present stimulation can arouse the desire.' And yet it must, I believe, be concluded that these memories in turn evoke some local response. We know from Pavlov's experiments that a local secretory response to the more direct appetite stimuli does occur, and it is not improbable that similar physical responses may be evoked by food-memories.

While contending that appetite is a complex and largely psychic phenomenon, modern observers have claimed a much more special character for the sensation of hunger, which Cannon and Washburne [3] and Carlson [4] have shown by the most careful experiments to be associated with and actually due to peristaltic contractions of the stomach. These they graphically recorded with the aid of rubber balloons and correlated with the hunger sensations. They admit, of course, that other sensations such as faintness and weakness may accompany prolonged hunger, but regard the actual hunger-discomfort as a gastric phenomenon. Is there any good evidence that appetite has also a local manifestation or a local cause? When asked to describe and locate the sensation of appetite people will provide the most variable answers, but there is a general tendency to refer it to the pharynx, the oesophagus, or the epigastric zone, and this reference seems to me to indicate that, as in hunger or the craving for food, so in appetite or the readiness for food there is a local process concerned. Subjective experience and clinical observation suggest that the local process may be associated with the tonic activity of the upper alimentary tract, much as hunger is associated with peristaltic activity; and that just as general well-being and

preparedness for physical effort are associated in idea and fact with a favourable state of tonus and adaptability in the skeletal muscles, so, too, digestive well-being and preparedness for gastric effort are associated with a favourable state of what might be termed 'anticipatory tonus' in the gastric musculature. Moreover, there is an undoubted association between the two states—that of general physical well-being and that of local digestive well-being. We know that nothing is more conducive to a good appetite than a healthy open-air holiday with plenty of exercise, or the procedure of training for an athletic contest.

In support of the view that appetite is partly a local process connected with visceral tonus, we have also clinical and radiographic observations of gastric function in certain general and gastric diseases associated with a poor or absent appetite. In conditions such as the debility due to prolonged fevers or accompanying tuberculosis and visceroptosis gastric hypotonus is a frequent finding. In gastric carcinomata which so infiltrate the wall of the stomach as to render it incapable of normal tonic and peristaltic activity, anorexia is present almost more constantly and in more pronounced degree than in any other malady, and as a symptom of the disease itself is as constant as pain.

This fact, that the most complete loss of appetite occurs in some diseases in which there is no impairment of the mental faculties and no interference with the special senses, is an argument in favour of the local appreciation of appetite being dependent on a local phenomenon.

If we wished experimentally to show a relationship between gastric tonus and the sensation of appetite, we should have to evolve a method of rendering the wall of the stomach rigid and incapable of tonic contraction and *adaptation, without modifying the other functions of the* body, without producing fever or the cachexia of malignant disease, and without inducing the debility which arises from pain or other physical or mental discomforts. Very occasionally Nature performs this experiment for us by means of the disease which has been variously described as linitis plastica, leather-bottle stomach, and cirrhosis of the

stomach. This condition is now regarded as cancerous, but in a small proportion of cases it seems that patients may live for months or even for years without the development of any severe pain, and without grave cachexia or dissemination of metastases. Profound loss of appetite may, however, be present.

I have seen one such case. A man in the forties had complained for two years of complete loss of appetite. He was leading throughout this period a most active life, both physically and mentally; he played games with vigour, but no measures which he could adopt and no treatment prescribed produced the slightest amelioration of his symptom. He did not experience pain, and his loss of weight was not more than would be accounted for by his diminished intake of food. On clinical and radiographic evidence a diagnosis of leather-bottle stomach was suggested, and was later confirmed at operation. As there is often no obstruction at any point, pain need not necessarily be a symptom in these cases, but hunger, which depends on peristaltic activity and appetite, which I believe to be in part an expression of gastric tonus, must both be inhibited.

Other conditions in which there is local damage to the stomach-wall with loss of appetite include pyloric stenosis when the stage of atonic dilatation has been reached, and alchoholic gastritis. In the former, tonus is obviously impaired. In the latter, although secretion and motility are deranged and the mouths of the gastric glands are blocked with mucus, the whole economy has been so much influenced by the prolonged poisoning that it would not be fair to assume that the anorexia was a direct expression of the local disease alone.

Have secretory abnormalities any influence on the sensation of appetite? There is, as a matter of fact, little evidence that the secretory behaviour of the stomach *per se* in any way modifies its sensations. Free HCl may be present in excess of the average or absent altogether in both healthy and unhealthy individuals without any gastric discomfort, and without appreciable modifications of hunger or appetite. Undoubtedly there is often a scanty, or even

an absent, secretion when anorexia is present, as, for instance, in cancer and gastritis, but we have better reasons for incriminating the impaired tonus and motility than the diminished secretion. Beaumont [1] showed that a very inflamed condition of the gastric mucosa with almost complete suppression of secretion might follow an alcoholic bout in the case of Alexis St. Martin without the production of any subjective symptoms.

Assuming that appetite may be in part an expression of healthy gastric tonus, and that it is at least a fair statement to say that impaired tonus and impaired appetite occur together, have we any evidence that hypertonus is accompanied by increased appetite? In many cases of duodenal ulcer, in which the stomach is demonstrably of hypertonic type, appetite is exaggerated, although for fear of aggravating their pain the patients may curtail their meals. It is also stated that the increased appetite and hunger of diabetes may be accompanied by the radiographic features of gastric hypertonus.

Briefly to summarize our knowledge in regard to appetite, I think we may say that *the sensation is in part a memory process and in part a local manifestation of efficient alimentary tonus reflexly induced by the memory stimulus, or by the more direct stimuli of seeing, tasting, or smelling food, or by some combination of these several factors.* This view helps to explain the close similarity between the appetite and hunger sensations as well as their essential differences, for tonic and peristaltic activity are kindred phenomena, but not synonymous.

Let us next consider the things which in health may modify appetite. Fresh air, exercise, cold weather, and a happy mind are amongst the important adjuvants, all being calculated to encourage an active and well-balanced metabolism. Conversely an indoor sedentary life and a heated atmosphere, or a worried or over-worked mind, are calculated to impair appetite, and in many cases actually do produce such a loss of appetite and general well-being as to amount to real ill health. The effect of certain emotions on

the appetite is pronounced. Falling in love, or a great bereavement, or a grave domestic or business anxiety, may for a time determine a real anorexia. Of these states, however, which come to trouble otherwise sound and healthy mortals, the majority are temporary and recoverable. The fatty and oily foods which inhibit appetite and may even cause nausea can be shown experimentally to be inhibitors both of gastric motility and secretion.

In reviewing anorexia as a symptom of established disease, some classification of causes becomes desirable. The following is, I think, as convenient as any:

Causes of Anorexia

1. Acute febrile illnesses.
2. Chronic infective illnesses, especially tuberculosis.
3. Other chronic debilitating diseases, especially malignant disease.
4. Local disease of the stomach, especially carcinoma and chronic gastritis.
5. Mental and emotional derangements, neurasthenic states, nervous dyspeptic states, and 'anorexia nervosa'.

Having drawn your attention to the frequency of lost appetite as a symptom in the mild as well as the graver types of disease, it might appear superfluous to compile such a special and limited list of causes. My reason is that in the types of disease included in this list, anorexia is a symptom of special importance from the diagnostic or prognostic point of view. In some instances, again, the treatment of the symptom itself may play a part in modifying the course of the disease, or even in producing a cure.

In the acute febrile illnesses there is a general arrest of many normal processes. The skeletal muscles become weak and flaccid; the secretions of the salivary, gastric, and other glands are diminished; the urinary output falls. The tissues are given over to measures of defence, and digestion and assimilation, except of water, are largely in abeyance. It is not surprising that the gastric musculature, like the skeletal musculature, should suffer fatigue and loss of tone,

and that the clouded senses should cease to be responsive to the stimulus even of the most carefully chosen diets. Thirst may be great, but the lack of appetite for solid food indicates the unreadiness of the stomach for ordinary digestive efforts. The moment, however, the infection is overcome we find a change in the sensations and inclinations of the patient. Very early in convalescence from pneumonia and still more after typhoid fever, the appetite improves and may even become voracious.

In chronic insidious infections such as pulmonary tuberculosis, loss of appetite may be of diagnostic as well as prognostic value. It is quite frequently an early symptom, and when we find a young adult with a tendency to easy fatigue, a waning appetite, a slight loss of weight—without other adequate explanation—we are always at pains to exclude or to discover a pulmonary lesion. In the more active phases of the disease anorexia is a well-recognized symptom. Both in the early and later stages there is a special tendency to loss of the breakfast appetite. When the night has been disturbed by sweats and the morning by cough and expectoration this is readily understandable; it is not quite so easily explained in the incipient or the semi-quiescent cases, but I have supposed that it here expresses the toxic-fatigue state following the evening auto-inoculation of the previous day. Those who work in sanatoria are familiar with the sometimes remarkable increase in the intake of food which is registered in those cases which are 'doing well' in respect of their general response to infection. This may be long before the physical signs point to appreciable local progress. Improvement of appetite goes hand in hand with stabilization of temperature and gaining weight. In a disease in which good nourishment is so vital it is obviously of the first importance to encourage appetite in every way, and in the good sanatorium the quality, preparation, and serving of the food are matters for special attention. In the late phases of disseminating malignant growth loss of appetite is almost the rule wherever the primary disease may have been, but the alimentary growths are more apt to promote the symptom. In carcinoma ventriculi anorexia

is, as I have mentioned, a very constant symptom, and according to Brinton [5] is present in 85 per cent. of cases. It may develop quite early (one patient told me that his earliest symptom was loss of appetite for bread), and I am inclined to think its degree bears a definite relation to the extent of stomach-wall involved. In every dyspepsia, but especially those which originate during or after middle life, inquire particularly about the appetite. This may occasionally help to differentiate growth from chronic ulcer. Generally in duodenal ulcer the appetite is good; in large lesser curvature ulcers and the mechanical obstructions resulting from scarring the appetite may become impaired; but it is rare in any of these conditions to meet with the complete abolition of appetite or positive aversion to food peculiar to gastric cancer.

In chronic alcoholism poor appetite is again familiar. It is most noticeable in the morning, and in bad cases may be associated with the equally familiar morning nausea, retching, and vomiting. When abstinence is observed and the gastritis is treated by lavage or other suitable measures there is a rapid recovery of appetite.

Some degree of anorexia is common in neurasthenia. By neurasthenia we should properly understand a condition of nervous exhaustion consequent upon physical or mental fatigue, fear, operations or illnesses or anxieties, or upon combinations of these. Having regard for the general loss of vitality and 'tone' in these cases, the symptom is one which we should expect. It may be an important one to treat, for the vicious circle of fatigue, loss of appetite, under-nutrition, and consequently more fatigue, may to some extent be broken by careful attention to the dietary. Cold beef appearing for the third day in succession may even discourage the hunter with his proverbial appetite, but for the limp and weary neurasthenic it can only buttress the misery of his existence. On the other hand, a dainty repast of small and well-cooked viands may do real physical good, and help to restore a little of the joy of living, or at least the will to recover it. Needless to say it is a small part of the treatment, but in a complaint for which there is no panacea

it is one of the many small parts which we cannot afford to neglect.

Among the writings of Sir William Gull [6], there are few more interesting than that which deals with the disease which he called anorexia nervosa. We are accustomed to think of the functional nervous diseases, harassing though they often are both to their victims and their physicians, as seldom actually dangerous to life. Here, however, is one which may lead to death from starvation, or to such emaciation as to recall the cruellest effects of war conditions or of famine. When we see our first advanced case of anorexia nervosa it may be impossible to believe that the sufferer has no underlying physical malady, and we are very properly anxious to discover signs of tuberculosis, diabetes, or other organic wasting disease. The subjects are mostly young women, but young men are not immune. There may be a personal or family history of emotional instability. We find that there has been for some time general failure of appetite, or at any rate a refusal to eat, often without any other striking subjective symptom. Various diagnoses will probably already have been suggested, and at the present day psycho-analytic methods may have been employed, with indifferent success or even with aggravation of the trouble.

The physical stigmata of anorexia nervosa, apart from the pronounced loss of weight, include an overgrowth of downy hair on the trunk and limbs, constipation, amenorrhoea, and a slow 'starvation' pulse. The mental stigmata include moodiness, resentment of maternal solicitude, and often a restless activity of mind and body which contrasts strangely with the poor physical state. Among 38 cases in my files, 35 were females. The common age-incidence is *between 15 and 25 years. Unhappy love-affairs, home* disagreements, and voluntary attempts at 'slimming' are recognized among the 'causes' of the disorder. Two-thirds of my cases were psycho-neurotics and gave no clue to suggest that the beginnings of their illness were physical. In one quarter the anorexia appeared to develop on the basis of an illness or an operation. The remainder were

psychotics. Recovery at home is rarely possible, but with removal to suitable surroundings, close supervision, and insistence on an adequate food intake, many of these cases may be restored to physical and mental health. In one case, seen with Sir Arthur Hurst, radiography showed the stomach to be peculiarly large and atonic. The patient made a complete recovery. It was judged unwise to repeat any investigations, so that we do not know whether gastric volume and tonus became normal again. It is not improbable that the local appearances in the first instance were evidence of a genuine atony induced by the prolonged mental and nervous depression and starvation.

Sir James Goodhart [7], in his lectures on the common neuroses, suggests that the term 'anorexia nervosa' might also be extended to those much more numerous sufferers from nervous types of dyspepsia. These patients commonly complain that they cannot eat this and they cannot eat that; their choice of foodstuffs is sometimes peculiar and irrational. They number among their ranks a host of nervous, voluble, sparrow-like women with sparrows' appetites. Personally I should prefer to keep the name 'anorexia nervosa' for the disease more clearly defined by Gull. Say that these others have a nervous anorexia if you like, but they seldom show signs of dying. Far from it. They will hop into your consulting-room and twitter forth their woes; they will neither gain weight nor appreciably lose it; they will try many treatments and ask for more. If you can, by some combination of severity and tact, persuade them to eat larger amounts of more ordinary food you may occasionally do them a real service. Their dyspepsias and anorexias are, I believe, more often due to or encouraged by under-nutrition than by any of the supposedly noxious foodstuffs or other factors which they themselves incriminate. The neurotic, like the neurasthenic, tends to eat too little, and, as he or she is commonly caught in a circle of evils, many of them hard for us to grasp, it is a comfort to have one point at which a rational attempt may be made to break the spell.

In the very young we encounter yet another variety of

functional anorexia. It affects the nervous children of anxious-minded parents, and is often largely to be attributed to the reputation for poor eating which the parents have repeatedly given them and conversed about in their presence. Being more plastic than adults and very suggestible, it is possible, with parental co-operation, to get them to eat well again by a simple process of judicious neglect, combined with the positive assurance afforded by telling others in their presence what good appetites they have. It is important, however, to remember that loss of appetite in children (just as in adults) may be an early symptom of physical disease.

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IX

CHRONIC DIARRHOEA[1]

For those of us who are chiefly concerned with clinical problems it is often profitable to discuss the natural history of a single symptom; to consider its several origins and types; and generally to pass in review the diagnostic difficulties to which it may give rise. Such a survey should include a valuation of the methods available for the investigation of the symptom, and should have as one of its aims the practical consideration of how to rationalize treatment. I have chosen as my topic chronic diarrhoea, under which heading may be included recurring or intermittent types of the complaint. I shall, wherever possible, base my remarks on personal clinical observations, referring only to such special or experimental work as seems to have a direct and useful bearing on the question. By diarrhoea we should imply—to quote a formula of J. Ch. Roux—'the too rapid evacuation of too fluid stools', in this way avoiding confusion with certain pseudo-diarrhoeas. So far as its actual incidence in practice is concerned, I imagine chronic diarrhoea would not, in our climate and at ordinary times, be regarded as a very common symptom. Nevertheless it is a symptom common to a great variety of diseases, and it may be a very troublesome one to analyse and treat. Furthermore, by reason of the wide extent of our Empire, increasing facilities for travel, and the ravages of war, certain types of infective diarrhoea have undoubtedly become more common in this country than they were in previous decades.

For the patient the symptom is mainly a subjective one—that is to say, it is the sensory discomforts and inconveniences which urge him to seek advice. It has, however, an advantage over more strictly subjective experiences in that it is accompanied by the passage of abnormal stools, with regard to the nature and number of which more or less accurate observations are possible. In no type of chronic

[1] *Lancet*, 1924, ii. 101.

diarrhoea can we afford to neglect such observations. Sometimes they declare or suggest the diagnosis at once. In all cases they give guidance as to the necessary collateral inquiries. There can be no doubt that modern perfections in domestic sanitation, however great their benefits, have served to hinder the modern physician, and to render him less familiar with the appearances of normal and abnormal faecal discharges than were his predecessors. It will be within the experience of many of us, too, that the sensibilities of the patient occasionally offer a strong resistance to our attempts to inspect a stool. For these and other reasons the routine inspection and special examination of faecal specimens have never received the thorough attention accorded to the urinary excretions. I shall have occasion to refer in more detail to this matter as my theme develops.

Classification

Before we can discuss the several types of diarrhoea and their differential features some form of classification is desirable. The best clinical classifications are usually those based on causal pathology. It so happens in the case of chronic diarrhoea that an anatomical classification of the sites of origin of the symptom is more convenient, and at the same time permits of a clear review of the underlying morbid processes. Thus, by considering in succession the stomach, the small bowel, the large bowel and rectum, and the accessory glands and structures communicating with the digestive tract (in particular the pancreas, the gall-bladder, and the absorptive apparatus comprising the lacteals and mesenteric glands) we cover the origins of all the important varieties of chronic diarrhoea, with the exception of those depending on external nervous stimuli or due to such complex factors as obtain in the case of Graves's disease.

Those due to nervous factors include a rare form of tabetic diarrhoea, diarrhoea due to reflex stimulation from a neighbouring visceral lesion, and emotional diarrhoea. To diarrhoea of gastric origin the term gastrogenous has been applied, and we might for brevity speak similarly of enterogenous,

cologenous, pancreatogenous, psychogenous diarrhoea, and so forth. Such adjectives, however, are open to criticism and do not adequately indicate the cause of the symptom. Diarrhoeas may also be broadly classified into those dependent upon functional digestive errors and those dependent upon organic and usually ulcerative intestinal disease. With most of us it will probably have been a natural inclination to regard diarrhoea as essentially a bowel symptom. It is, however, no more essentially a symptom of primary bowel disease than tachycardia is a symptom of heart disease, or dyspepsia of stomach disease. At the outset, therefore, the classification which I have suggested reminds us of the necessity in the individual case of reviewing widely diverse possibilities, and of arranging our interrogation of the patient in such a way as to obtain information relating to the functions of many parts.

Methods of Investigation

Assuming a careful history to have been taken and a routine overhaul made, it becomes necessary to consider what special examinations should be conducted in a given case. These examinations may be usefully subdivided into (*a*) essential clinical examinations; (*b*) valuable and often essential accessory investigations which yet fall within the scope and province of the clinician; (*c*) special examinations for which it is usually preferable to obtain the co-operation of an expert in chemical, bacteriological, or radiographic methods.

The essential clinical examinations include inspection of the stools and a rectal examination, and should, strictly speaking, be omitted in no case of chronic diarrhoea.

The accessory investigations falling within the province of the clinician, but in which he may sometimes elect to obtain co-operation, include a direct inspection of the *rectum or sigmoid through a proctoscope or sigmoidoscope*; a simple *microscopic* examination of the stools for blood, pus, meat-fibres, &c.; a chemical examination of the stools for the presence of blood, or of a filtrate of the stools for albumin; and occasionally the examination of a blood film.

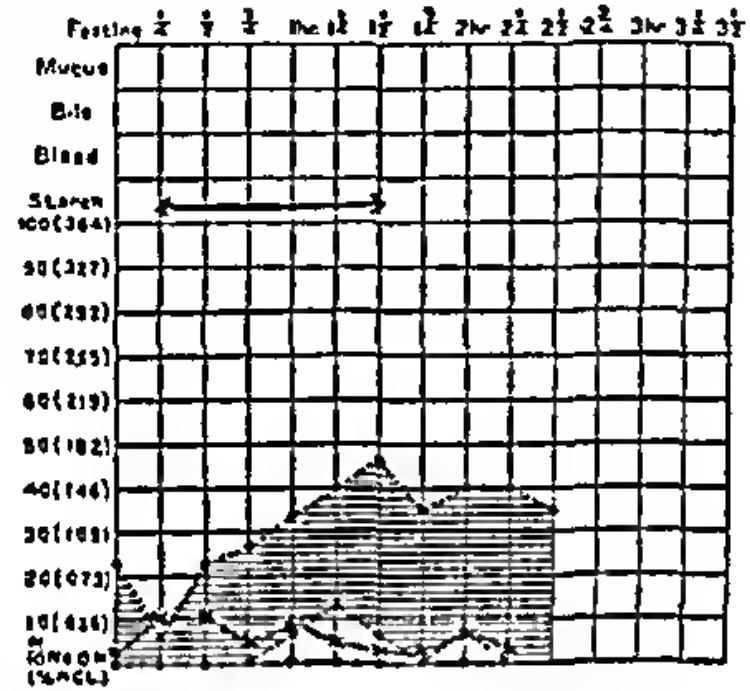
anaemia, and splenic enlargement or a history of sore tongue or of sensory manifestations pointing to central nervous disease should be seriously regarded.

A fractional test-meal in the majority of cases shows complete absence of free acid throughout the meal, and a very low curve of total acidity. Usually there is rapid emptying, the stomach sometimes being void within a half to three-quarters of an hour instead of in the more usual period of two hours. A radiographic examination with an opaque meal shows a similar rapid emptying and rapid passage throughout the intestinal tract. This rapid evacuation of the stomach, with consequent over-stimulation of activity in the small intestine (and possibly inadequate stimulation of the pancreas) is the likely cause of the diarrhoea. The therapeutic test of giving acid may be an important diagnostic point when other methods of investigation are not available.

The treatment includes, where possible, the removal of any likely cause of a secondary achlorhydria, such as alcoholic excess or dental sepsis. An alcoholic diarrhoea, perhaps more commonly seen in beer-drinkers than spirit-drinkers, will improve or clear up altogether if the patient succeeds in altering his habits, and it can be shown that an achlorhydria may under these circumstances be replaced by a normal secretory curve. In gastrogenous diarrhoea doses as small as 10 or 20 minims of the dilute preparation of hydrochloric acid three times a day may be successful in checking the frequent evacuations, and it is rarely necessary to give more than 30 minims. Taken with lemonade or orangeade with the three main meals it is quite a pleasant beverage. I have also seen one or two cases of chronic diarrhoea, apparently of gastric origin, in *which complete relief followed the taking of acid, notwithstanding* that gastric analysis gave normal figures.

The following case is instructive. In the early stages the patient's symptoms were those of a simple gastric diarrhoea, but were not recognized as such. Later he developed Addison's anaemia. The accompanying chart illustrates the test-meal findings characteristic of both conditions.

A middle-aged man came under observation on account of severe anaemia, with a history of breathlessness and failing strength of about one year's duration. For nine years he had been troubled by a chronic painless type of diarrhoea. Seven years previously an X-ray examination had shown a rapidly emptying stomach and exceedingly rapid evacuation of the barium. The blood picture was typical of Addison's anaemia, and the fractional test-meal showed complete achlorhydria. Within 24 hours of starting to take hydrochloric acid the diarrhoea was entirely controlled.



Diarrhoea after Gastro-enterostomy

One other type of gastric diarrhoea resulting from unsuccessful or too successful surgery deserves mention. From time to time one sees patients who have had a gastro-enterostomy performed, and have thereafter developed chronic or intermittent diarrhoea. There are two types—a benign one which is fortunately the more common, and a rare one associated with other and graver symptoms. The benign type closely simulates the simple gastric diarrhoea already described. It is due to a too patent stoma causing excessively rapid emptying, with the result that there is no time for gastric digestion to take place. There is over-

neutralization of the gastric juice, and consequently an artificial achlorhydria; pancreatic secretion, and certainly exposure to pancreatic secretion, may also be inadequate. The stools are light in colour, and may show fatty crystals and meat fibres, but no blood. There is no pain, but there is often discomfort referred to the small bowel area surrounding the navel and occurring almost immediately after food. In a case of this kind recently under my care the patient had once noticed fragments of egg-white in the stools within half an hour of their ingestion; X-rays showed the stomach to be empty in ten minutes; test-meal showed achlorhydria, and the stools contained soaps, fatty acids, and meat fibres in excess of normal. Dry meals, lying down after the main meals, and the administration of acid (provided there is no persisting evidence of gastric, duodenal, or jejunal ulceration) often give relief.

The serious type is due to the development of a gastro-jejuno-colic fistula as the result of secondary ulceration. In such cases pain, great emaciation, foul eructations, vomiting of faecal matter, and anaemia may be present in addition to the diarrhoea, and gastric acidity is likely to be high.

Diarrhoea Originating in the Small Bowel

There is only one important cause of diarrhoea in this group—namely, tuberculous ulceration of the ileum. For this reason diagnosis should seldom be in doubt as (excepting in the far less common variety of localized ileo-caecal tuberculosis) there is nearly always active coexisting lung disease or generalized abdominal tuberculosis. The frequency of the calls to stool is very variable, and it should, of course, be recognized that ulceration may be present with constipation. Generally the frequency bears some kind of relation to the extent of the disease. A common story is four to six actions daily—a rather higher average figure than in most cases of gastric diarrhoea, but a lower one than obtains in ulcerative lesions of comparable severity in the large bowel. In contradistinction to the gastric group pain is a frequent and troublesome association. It is usually referred to the peri-umbilical and right iliac zones, and

tenderness in the right iliac fossa is commonly present. There is the same post-prandial tendency to looseness as in the diarrhoeas of gastric origin, and hot soups and fluids are especially disturbing. The stools are soft or semi-fluid, and light in colour. It is rare for macroscopic blood or mucus to be present, but positive results with the benzidine, guaiac, and spectroscopic tests are obtainable. If the ulceration be very extensive, and particularly if there be much involvement of the mesenteric glands causing obstruction to the lymphatic flow, the stools may be copious and chalky-looking and contain excess of fats and soaps, while in virtue of the diarrhoea undigested meat fibres are present. With appropriate technique tubercle bacilli can also be demonstrated.

Treatment in these cases can only be palliative, but Gull [4] pointed out as long ago as 1855 the importance of avoiding the then common practice of giving cod-liver oil or a diet rich in milk and cream in cases of tuberculous disease in which fat absorption is at fault. Cases of diarrhoea due to a non-specific enteritis persisting long after an attack of food-poisoning are occasionally seen and may be very resistant to treatment.

Diarrhoea Originating in Disease of the Colon and Rectum

This is a most important group, and is more beset with difficulties than either of those to which I have referred. It includes the chronic phases of amoebic and bacillary dysentery, other forms of infective ulceration of the colon of unspecified origin, non-ulcerative types or stages of colitis, malignant ulceration of the colon and rectum, the terminal colitis of Bright's disease, certain spurious forms of colitis and diarrhoea, such as that which is commonly classified as 'muco-membranous', and those due to constipation, abuse of purgatives, and excess of douching. In this group more than in any other careful rectal examination, direct inspection of the mucosa through a sigmoidoscope, and macroscopic and microscopic examinations of the stools are of importance. It is in this group that serious

mistakes are made through omission of simple examinations. It will probably have been within the experience of many of us to discover a rectal carcinoma, primarily regarded and treated, sometimes for months, as a case of 'diarrhoea', 'colitis', or 'piles'. I see two or three such cases every year. And there are other pitfalls; I have, for instance, in the last two years seen three patients who had at some previous date suffered from dysentery or ulcerative colitis, but in whom a carcinoma of the colon had subsequently developed and been missed in spite of careful investigations. The old story of colitis or dysentery had served to lull suspicion instead of rousing it, for there is, I believe, a definitely increased liability to malignancy in persons who have previously suffered from chronic infective ulceration of the large bowel.

In a considerable proportion of all cases of diarrhoea from active colonic or rectal ulceration, from whatever cause, blood, mucus, and sometimes pus will have been observed by the patient himself at some period of his illness. So long as ulceration persists blood will be demonstrable microscopically and chemically, if not macroscopically, for the cells have not, as in bleeding at a higher level, had time to undergo disintegration. Leucocytes much more readily undergo disintegration, and for this reason their presence in large numbers points to a lesion low down in the large bowel or to an abscess discharging thereinto. Goiffon [5] states that albumin in the filtrate from a faecal emulsion is a reliable index of the presence of active bowel ulceration, but I have not employed the test myself. Pain, both colicky and (if there is extensive inflammation of the wall of the bowel) more continuous, and accompanied by tenderness, is a frequent but not constant association of all ulcerative forms of colitis. It is commonly referred to the lower abdomen, and especially to the region of the descending colon and rectum, and is most in evidence during or after defaecation. The diarrhoea may be continuous or intermittent and, particularly in cases of malignant disease, may alternate with constipation. In an acute phase the evacuations are frequent and small, and consist largely of blood,

mucus, and sometimes pus. In the more chronic phases they may be watery and intermixed with faecal material, the blood and mucus being less conspicuous. With growths low down in the colon and in the rectum the blood may sometimes be so intimately mixed with a watery brown malodorous evacuation as to escape the patient's notice. When not sufficiently obvious on a casual inspection blood and mucus can often be made apparent by gently tilting the bed-pan—a receptacle which should always be employed in preference to others in suspicious cases; the viscid mucous fragments are then seen to slide more slowly across the white field than the fluid elements of the stool. Washing with water may also bring abnormal particles to light.

The Dysenteries

In the case of the dysenteries it is important to recognize that both varieties (but more rarely that due to *Entamoeba histolytica*) may be acquired in this country, and that relapses after periods of good health are common. Of the two the amoebic variety is the more likely to give rise to a chronic mild diarrhoea with little or no pain. The asylum dysenteries have been shown to be generally due to bacillary infections, and Sir Arthur Hurst [6] has suggested that a considerable proportion of the sporadic cases formerly classified as 'ulcerative colitis' are in reality chronic bacillary dysentery. From the point of view of the morbid changes in the mucosa no distinction can be drawn between chronic bacillary dysentery and chronic 'ulcerative colitis', and a certain proportion of cases of the latter show a very remarkable response to treatment with polyvalent anti-dysentery serum. When it is remembered that only a comparatively small proportion of acute bacillary dysenteries give positive cultural results it is no cause for surprise that chronic cases are generally negative from the bacteriological standpoint. This uncertainty in laboratory diagnosis renders a direct visual examination of the diseased surface all the more important. So valuable diagnostically is the appearance of the local lesion that a digression on the application of

sigmoidoscopy in all forms of colitis, whether suspected of belonging to a surgical or medical category, may, perhaps, be pardoned.

Although, as with other endoscopic instruments, technical difficulties are encountered from time to time, no special manipulative skill is necessary for the use of the sigmoidoscope. It is a simple instrument and, with practice and due care, its employment entails little or no risk. Unless there is ulceration of the anal canal or a concomitant pelvic inflammation its passage—though uncomfortable—is practically painless and an anaesthetic is seldom necessary and should preferably not be given.

Unless general weakness or special circumstances forbid, the patient should be examined in the knee-elbow position. There should be as little preparation beforehand as possible, and the clearest views are often obtained in patients who have simply been instructed to get up and empty the bowel voluntarily two or three times in the few hours before the examination. Purgatives are best avoided altogether, but simple preliminary lavage may be necessary. A hypodermic of morphine, 20 minutes before the examination, serves to allay anxiety and to lessen peristalsis. After the first few inches are passed the instrument must be guided visually.

In *ulcerative colitis and chronic bacillary dysentery* all phases between a granular mucosa with a tendency to bleed easily and extensive, but usually superficial, ulceration may be seen. The ulcers, except in very severe types, are shallow and their margins are not raised or undermined. The intervening mucosa is never healthy, appearing red, swollen, and easily bleeding. A film of muco-pus frequently covers the ulcerated areas. In cases of long standing a condition resembling a generalized polyposis may develop.

In the chronic forms of *amoebic dysentery* seen in this country it is rare to find extensive ulceration; but the appearances, though often slight and inconspicuous, may be completely diagnostic. The ulcers are usually quite minute and round and appear as tiny central craters in a small elevation of the mucosa. The craters may be empty or contain a yellow slough, in which case they are not unlike

sometimes accompany chronic constipation and the prolonged nbuse of purgatives.

The picture of muco-membranous colic is a familiar one. It occurs in women of a particular nervous type in whom chronic anxiety and depression have developed in relation to the state of their excreta aod many other things; they are generally of sallow habit and have dark skins; they suffer much from nbdominal pain referred especially to the descending colon, which may be unduly palpable as a hard cord; their evacuations are too frequent and they often say that they have diarrhoea. Strictly speaking, the stools are too fluid only to the extent that they are passed in association with large quantities of coagulated mucus often in the form of long casts. If examined carefully and at a time when purgatives are not being taken, it will generally be found that the faeces are fragmentary and constipated. Blood and pus are absent, and the mucous membrane appears normal or only slightly red through the sigmoidoscope. The condition is really one of *spasmodic* constipation, and the large quantities of mucus are the result of irritation and oversecretion rather than of actual inflammation. If treatment with purgatives or douches has been carried out over long periods, or there has been much faecal retention, a true irritative colitis with diarrhoea may be superadded. With chronic rectal constipation or dyschezia, erroneously treated with salts or irritating laxatives, it is not uncommon for small ineffectual fluid stools to be passed, but rectal and abdominal examination will disclose an accumulation of scyhala in the lower bowel, and discontinuance of the purgative medicines and the institution of rational hygienic measures should relieve the condition.

Diarrhoea Due to Disease of the Pancreas

Bright [7] was the first in this country to draw attention to the occurrence of fatty diarrhoea in certain cases of carcinoma of the pancreas involviag the duodenum. Pancreatic diarrhoea is actually a very rare condition, although, mainly on the strength of laboratory reports, it has been a common diagnosis in the presence of steatorrhoea. The chief

feature of the stools in a true pancreatic diarrhoea is the passage of fat in the shape of oil or a fatty coagulum, or of oil which later congeals as a fatty layer. Microscopically fat globules are shown and undigested meat fibres and starch are also present. The diastase test in the urine, or glycosuria, may give further evidence of impaired pancreatic function. Carcinoma, calculi, and chronic pancreatitis are among the conditions in which a true pancreatic fatty diarrhoea has been described.

Fatty or Chylous Diarrhoea from Disease of the Absorptive System

There is, however, another important cause of fatty diarrhoea, as Gull [4] originally pointed out, in which the fat is passed intimately mixed with the stools and is largely present as split fats, appearing under the microscope as crystals and soaps. The stools under these conditions are very bulky, in some cases almost incredibly so. They are pultaceous, pale or greyish in colour, greasy and rancid, and they may froth like soap when water is poured upon them. The absorptive apparatus includes the intestinal mucosa and the lacteal tree. Gull recorded the occurrence of fatty stools of this type in tuberculous disease of the mesenteric glands, and Lecture X is concerned with similar cases in which in the course of a laparotomy the lacteals were actually seen to be enormously distended with chyle, owing to obstruction by caseous glands in the mesentery. Other conditions in which stools of similar character may be encountered include the so-called coeliac affection in children, tropical sprue, idiopathic steatorrhoea (non-tropical sprue), and occasional cases of gastro-colic fistula and abdominal malignant disease. In sprue and coeliac disease other symptoms which may accompany the fatty diarrhoea of tabes mesenterica (such as tetany due to the excessive excretion of calcium) are also recorded, and I have, therefore, put forward the suggestion that the diarrhoea in all these conditions will probably be found to be due to obstruction of the lacteals by some other non-tuberculous disease of the mesenteric glands.

The treatment of all cases of fatty diarrhoea in which faulty absorption is suspected should include rigid fat restriction. It is remarkable what improvement in respect of the diarrhoea, weight, general nutrition, and other secondary symptoms may follow this simple procedure.

Simple Diarrhoea accompanying Mesenteric Glandular Tuberculosis

In addition to a true fatty or chylous diarrhoea, we should also recognize a simple form of mild chronic diarrhoea with passage of light-coloured stools, which is among the earliest symptoms in tuberculous disease of the abdominal lymphatic glands. The symptoms may be present long before the abdomen becomes appreciably enlarged or without other classical signs of tabes mesenterica ever appearing. I have seen several cases of this type in which further investigations strongly supported a diagnosis largely prompted by this symptom. The condition is practically confined to children and young adults. The following is a case in point:

A small girl, aged 11, was brought to see me on account of attacks of lower abdominal pain. For some time past her mother had noticed that she was having her bowels moved too frequently. The stools were reported as loose and light in colour, and this was confirmed on making a rectal examination. Her mother and teacher had both observed that she easily became tired, and she often went to bed on her own initiative long before her usual bedtime. The pain in the attacks was referred to both iliac fossae—a common reference in these cases. I suggested keeping her under observation at home, with morning, afternoon, and evening temperature records. The five o'clock mouth temperature (the hour at which she often wanted to go to bed) was found to be nearly always 99 or above, and on one occasion it was 100. X-ray examination of the thorax showed shadows of numerous small calcified glands at the hila, and considerable peri-hilar infiltration. Rest in bed, with a diet in which fats were kept low, resulted in a steady gain in weight and a cessation of the diarrhoea. The daily swing of temperature steadily diminished. There were no further attacks of abdominal pain. At no period were any of the characteristic signs of tabes mesenterica present.

It is improbable that the diarrhoea in these cases expresses ileal ulceration; I suspect that it signifies again a fault of absorption due to glandular disease, but of a

lesser degree than that encountered in the occasional cases of fully developed chylous diarrhoea. The diarrhoea of lardaceous disease—now so rarely seen—probably depends on faulty absorption due to amyloid changes in the intestinal mucosa.

Diarrhoea in Chronic Cholecystitis

In chronic mild infections of the gall-bladder, persistent or intermittent diarrhoea of a mild grade is a not uncommon complaint. The associated symptoms include epigastric or right subcostal pains and discomforts; a dyspepsia of which nausea and right subscapular or interscapular pain are frequent features; vague general ill health; a tendency to unexplained spikes of pyrexia with other manifestations peculiar to chronic infections of the upper alimentary tract. There is usually tenderness at the gall-bladder point. I am not sure whether the diarrhoea in these cases should be regarded as a reflex diarrhoea akin to the accompanying reflex dyspepsia, or as an expression of the general upper-tract infection, or possibly of the achlorhydria which is found in a certain proportion of such cases. The treatment is the treatment of cholecystitis. If gall-stones are not suspected and there is no sufficient indication for surgery it should in the first instance comprise general hygienic and dietary measures, and the administration of biliary antiseptics such as urotropine and salicylates.

Diarrhoea Due to Organic Nervous Disease

I do not propose to discuss tabetic diarrhoea. French authors, of whom Timbal [9] mentions several, have described a true diarrhoea in tabes, but I have not personally seen a case. The only one in my experience in which the diagnosis might have been entertained did not conform to Roux's definition; that is to say, although the patient—an undoubted tabetic—complained of distressingly frequent and urgent calls to stool, she did not, so far as I could ascertain, pass 'too fluid' stools, and more often than not she passed nothing at all. The symptom was, in all probability, due to true rectal or colonic crises. It had been

present for many years, but latterly a change in its character had raised the possibility of carcinoma coli. I did not have the opportunity of investigating the matter further.

Reflex Diarrhoea

The following case illustrates a type of diarrhoea which may I think, legitimately be described under this heading. Cases in which there is an actual appendicular or pelvic abscess should not be included in the same category, for in these the sepsis and peri-rectal inflammation are the more important factors.

A medical man who had had bacillary dysentery during the War started in 1919 to have diarrhoea with frequently recurring exacerbations, associated with much pain of a colicky character, but a complete absence of localizing signs. There was pyrexia during the attacks. Various investigations were made with negative result. No treatment had any effect. A very thorough investigation in a clinic between attacks was quite unproductive, and in 1922 it was finally decided to perform a laparotomy. A thickened inflamed appendix was removed, which contained about half a cubic centimetre of pus. There was no subsequent return of the attacks. The appendix was 'silent' in so far as the production of symptoms directing attention to itself was concerned, but had produced such definite bowel symptoms as colic and diarrhoea.

Emotional Diarrhoea

The nervous diarrhoea which I wish more particularly to stress expresses an anxiety-state, but it is important to recognize that it may develop on the basis of a true irritative or infective diarrhoea. All grades of it are encountered. One individual may have a mere tendency to diarrhoea at the ordinary times of defaecation or on special stressful occasions—as before a viva voce examination; another unfortunate may so far lose confidence in himself and his power to control the activity of his bowel that it becomes impossible for him to go to any social function or to expose himself to any conditions under which self-consciousness is likely to prevail. To have to face the risk of being out of reach of a lavatory on these occasions becomes for him an insufferable anguish. The condition is a visceral neurosis closely akin to nervous bladder frequency. Like stammering

The correctness of the diagnosis cannot be dogmatically asserted in every one of these cases, but all were carefully reviewed, and most of them were very thoroughly investigated. Sometimes more than one factor may be at work. I have, for instance, seen a case (not included in this series) in which a relapse of ulcerative colitis was associated with gastritis and achlorhydria, attention being drawn to this by the presence of acne rosacea.

I hope that I have said enough to indicate the great diversity of conditions which may give rise to chronic diarrhoea, and to suggest the methods most likely to be of service in their differentiation. I have dealt with the question of treatment superficially, but it must be my excuse that diagnosis is the beginning and the end of medicine, and an essential preliminary to rational therapeutics.

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to be well founded, though it is probable they often mistook inflammatory exudation for chyle. Modern authors have passed over the subject, or have treated it lightly.

'The normal absorption of fatty matters is prevented from two causes; either from a defect in the digestive or emulsifying process, or from disease of the absorbent system. The instances of fatty stools from disease of the pancreas and the duodenum, as described by Dr. Bright and others, belong to the former, and are characterized by the fat passing from the intestines, more or less separate from the general mass of the faeces, and concreting upon them; but in the latter case, where the disease is in the absorbent system, the fat, *being emulsified, becomes incorporated with the evacuation, and is consequently not so easily recognized.* If, however, there be, with defective absorption, an inflammatory condition of the mucous membrane and diarrhoea, the oily matters rise to the surface of the evacuation as a creamy film, and produce the pale, chalky, and soapy appearance so characteristic of chronic muco-enteritis and mesenteric disease.'

In describing a case of fatty diarrhoea due to tuberculosis of the mesenteric glands he says:

'The bowels were generally moved three times in the twenty-four hours. The evacuations were pultaceous or liquid, of a dull chalky colour, frothing like soap when a stream of water was poured on them. Under the microscope they were seen to contain muscular fibre in different stages of disintegration, starch cells, &c., and finely divided oily and granular matter like chyle, and inflammatory exudation.'

We can add little if anything to Gull's conclusions as to the main causes preventing 'the normal absorption of fatty matters'. The interest which has been stimulated in recent years in the various special tests for pancreatic efficiency would seem, on the experience of the cases described hereunder, to have blinded us somewhat to the value of the simpler methods of observation and deduction employed by 'the older physicians'.

During the past three years I have had the opportunity of studying two cases of fatty diarrhoea in adults, and one in a child. In both of the adult cases, in spite of careful clinical and laboratory investigations, the true cause of the condition escaped recognition prior to the performance of a laparotomy, and a diagnosis of pancreatic disease had been entertained.

It should, I believe, have been possible in each instance

to predict the correct diagnosis on clinical grounds. I have therefore thought it worth while to place on record an account of the cases in question. In doing so I am further actuated by the fact that Case I showed features so characteristic of what has been described as the coeliac disease in children that I hoped that it might serve to throw some light upon the causal pathology of that obscure malady.

CASE 1. A young woman, aged 23. Admitted for chronic diarrhoea and tetany. Since she was a baby she has been subject to attacks of diarrhoea. In recent years these have become more continuous, and latterly there has been little or no intermission. Often she passes six or more fluid stools a day. The diarrhoea is associated with pain above the umbilicus. In spite of this prolonged ill health she has a good appetite and has not lost weight. When overtired, and invariably during the menstrual periods, she has attacks of true tetany with carpo-pedal spasms. These have been becoming worse and more frequent; last from 2 to 6 hours; and are relieved by morphine. Her doctor (Dr. H. L. Burton) thinks they have been fewer while she has been taking parathyroid tablets. She looks younger than her years; is of small stature; and has a 'pink and white' complexion, with small dilated venules on the cheeks. The whole abdomen, but especially the lower part, is rather full and tense. The abdominal reflex is brisker on the right. *The stools are enormously bulky, frequently filling almost half an ordinary bed-chamber as the result of a single evacuation. They are rancid, greyish, and porridgy in consistency. They show excess of fatty matters and meat fibres. Under the microscope crystals and soapy fragments were observed.* Quantitative estimations of the fat in the stools were not performed.

Subjective symptoms improved as the result of rest. Pancreatin was given without effect.

A few weeks after she came under observation tenderness developed in the right iliac fossa, and it was decided to explore the abdomen. The operation was performed by Mr. L. Bromley, who reported as follows: 'The appendix was adherent to the lower end of the mesentery. It was removed and found to show a few scattered submucous haemorrhages, and contained a bead of pus at its tip. The mesentery of the small intestine contained innumerable caseating tuberculous glands. *The lymphatics were looped and tortuous, white in colour, being distended with fat droplets, the passage of which was obstructed by the condition of the mesenteric glands.*' The distended lacteals indeed presented a remarkable appearance, their calibre in places almost equalling that of a tooth-pick. Their condition at once explained the nature of the long-standing fatty diarrhoea.

The patient was treated for about a year with rest, open air, and a diet as nearly as possible fat-free. For a time there was abdominal

discomfort and pain, and a small fluctuating area near the umbilicus, presumed to be due to breaking-down glands, developed. Radiographic evidence of peribronchial glandular tuberculosis was also forthcoming, and for a time some patches of lichen scrofulosorum were present on the skin. On the fat-free diet the stools became formed and darker in colour, and were reduced to one or two per diem, but they still remained abnormally bulky.

Finally the patient's general condition improved greatly, and she has now been actively employed with light duties for many months. There is no actual diarrhoea. Minor tetanic spasms have recurred from time to time. Calcium is now being given in an attempt to control this symptom.[1] Throughout the whole period of observation the temperature only very rarely rose above normal. (Many years later, after a life of fluctuating invalidism always cheerfully borne, this patient died in one of Sir Arthur Hurst's beds at Guy's from an oesophageal carcinoma. At the necropsy confirmation of the original diagnosis of tabes mesenterica was obtained.)

It is difficult to avoid the conclusion that this patient had a condition of tabes mesenterica dating from early childhood. For six years, at any rate, she had been subject to tetany, and the diarrhoea started many years before this. Nevertheless, appetite and general nutrition had been good on the whole, and she had been working hard before coming under observation.

The tetany was presumed to be associated with periods of acute calcium deficiency resulting from the excessive excretion of calcium soaps; it was consequently worse when the diarrhoea was worse, and disappeared when the diarrhoea was relieved by giving a fat-free diet.

The features which might have helped to establish the diagnosis were: (1) the naked-eye appearance of the stools, which were of the bulky, greasy, pultaceous type described by Gull, and contained no separate oil or coagulum; (2) the presence of crystals and soaps, suggesting that absorption rather than digestion was chiefly at fault; and (3) the tetany, which presumably should not occur with the passage of unsplit fats as in true pancreatic deficiency.

The presence of meat fibres merely expressed the diarrhoeic state.

[1] 5.12.23. Within 48 hours of starting calcium lactate, gr. x, three times daily, minor facial and carpal spasms, present for some time, have ceased. Chvostek's sign, however, is well marked.

Case 2. A man, aged 36. Admitted for great loss of weight, hunger, thirst, abdominal fullness, and the passage of copious light-coloured stools. Previous history: Feeble at birth, and before the age of 17 had pneumonia, tuberculous glands in the neck, tuberculous disease of the left ankle-joint, and an operation on the left mastoid antrum. After the age of 18 he became very fit. He was always a very large eater, but his food did not seem to fatten him. One sister has pulmonary tuberculosis. He joined the Army during the 1914–18 War and served in France, Egypt, and Salonika. Appendicectomy at Salonika in 1915. In 1920 he went to Canada. At this time he was feeling rather weak and had 'acidity' and lower abdominal discomfort about 1 hour after meals. Next summer he went away for a holiday, and lived on farm produce, but the acidity and fullness increased rather than diminished. In September 1921 he had violent diarrhoea and passed ten motions a day 'of the colour of modellers' clay'. He was investigated in Toronto, and a diagnosis of 'hyperacidity' was made. Another physician said he had phthisis, and a third dysentery. He managed to remain at work, but felt very ill and passed three stools a day.

In April 1922 he came to England and was re-investigated in London. As the result of various examinations, and particularly on the strength of the presence of fatty globules, fatty acids, and meat fibres in the stools, he was regarded as having pancreatic disease. He made no improvement with pancreatized food or pancreatin. In August 1922, as he was making no headway, an exploratory laparotomy was performed by Mr. Cecil Joll. A condition of tabes mesenterica was revealed, and, as in the other case, the lacteals were seen to be enormously distended.

On admission in January 1923 for further observation he was terribly emaciated, his weight having fallen from 10 to 7 stone in 2 years. The abdomen was greatly distended and tympanitic. He was suffering from an abnormal hunger and thirst. He expressed himself as fond of fats, cream, butter, and savoury jellies.

With a fat-free diet, liberal fluids, and pituitary injections to control the meteorism, some temporary improvement was achieved, but it was only too apparent that in addition to lacteal obstruction from glandular disease the patient was also suffering from tuberculous ulceration of the intestine, and he did not long survive.

In this case, as in Case No. 1, the fallacy arose of supposing that fat and meat fibres in the stools must necessarily indicate pancreatic deficiency. The fat in each case was due to faulty absorption from obstruction of the lacteals, and the meat fibres were merely an expression of the diarrhoea.

Although chronic or intermittent diarrhoea with light-coloured stools is a well-recognized symptom of tabes

mesenterica, manifestations of the character and severity seen in Cases 1 and 2 must, I think, be rare.

So similar are the main symptoms recorded in Case 1 to those recorded in cases of coeliac disease, that I would submit that the causal pathology of coeliac disease cannot be regarded as fully investigated until it has been demonstrated at operation or post-mortem that there is, or is not, some obstructive lesion in the lacteal system or the thoracic duct. The lesion is most likely to involve the mesenteric glands. In none of the post-mortem examinations in cases of coeliac disease referred to by Still [5] and by Miller [6] is any specific mention made of the state of the lacteals. The fact that the lacteals may be seen to be distended at operation on a patient taking a normal diet does not necessarily imply that they should remain visibly enlarged after death in patients who have been on a low diet and have died of some terminal infection. The lacteals were not stated to be so distended after death in the case reported by Gull, the clinical description of which closely conforms with the description of Case 2. Evidence of tuberculosis has been consistently lacking in fatal cases of coeliac disease, but lymphatic obstruction need not necessarily be the result of tuberculosis. In fatal cases of fatty diarrhoea reported by Poynton and Paterson [8] and by Whipple [9] there was gross non-tuberculous enlargement of the mesenteric glands, and in Whipple's cases the glands, which were fibrotic, and the intestinal villi were packed with deposits of neutral fats and fatty acids.

Miller, who is responsible for several important contributions to the study of coeliac disease, claims that there is not sufficient evidence to indicate that the failure to absorb fats is due to any lesion of the intestinal mucosa. He concludes [6] 'that coeliac disease is independent of organic changes and thus must be due to a digestive fault (probably a defective action of the bile on fat-absorption)'. That such a gross derangement can depend upon 'a defective action of bile on fat-absorption' alone, when there is no evidence forthcoming of hepatic, biliary, or pancreatic disease, seems to me to be an untenable hypothesis.

To replace it I would therefore put forward the suggestion that *the inability to absorb fats in coeliac disease, and the attendant complications, such as infantilism and tetany, can best be accounted for by an obstructive lesion (probably infective in origin, as the disease is acquired and not congenital) of some part or parts of the lacteal tree.* The severity of the condition probably bears some relation to the amount of the obstruction, and in Miller's non-diarrhoeic cases [7] it would be reasonable to suppose that there is less involvement of the mesenteric glands than in the fully developed type of the disease. On this hypothesis also the slow recoveries from coeliac disease might be held to be due in part to the establishment of a collateral lymphatic circulation, and the generally prompt improvement on a fat-free dietary to relief from overpressure of chyle in the already choked lymphatic tributaries.

Gee [10], in his original account, apparently draws no distinction between the coeliac disease of infants and those tropical cases of fatty diarrhoea which we now classify as Sprue. Manson-Bahr [11], in describing the morbid changes found in sprue, says, 'The mesenteric glands are generally large and pigmented, perhaps fibrotic.' He also mentions the occurrence of tetany in chronic cases. Recently attention has been drawn by T. H. Jamieson [12] to the good results obtained with a fat-free dietary in sprue, while H. H. Scott [13] has demonstrated calcium deficiency, and commends the use of calcium lactate and parathyroid. It seems highly probable that the tetany and calcium deficiency which occur in some cases both of coeliac disease and sprue may be connected with the excessive excretion of calcium soaps, as in Case 1. Distended lacteals have also been seen during the performance of laparotomy in cases of sprue.

The following case of infantilism and late rickets displayed features strongly reminiscent of coeliac infantilism. The blood-calcium was deficient, and although diarrhoea was only occasional there was excess of fat in the faeces. The patient also showed clinical and radiographic evidences of tuberculosis, and I consequently suggested a diagnosis of old mesenteric glandular tuberculosis causing faulty fat-

absorption, and so contributing to the retardation of growth and the rickety bony changes.

Case 3. A girl, aged 15, was admitted for 'arrest of growth, deformities, and intestinal troubles'.

At the age of 3½ years she had a febrile attack accompanied by the passage of loose grey motions. Attacks of this type have recurred three or four times a year ever since. At 10 years she only weighed 4 st. 5 lb. Her appetite has always been poor, and she will not touch milk. The stools have varied in character from day to day, but except in the attacks there is no diarrhoea. Patient is small, and in bulk and stature resembles a child of about 8 or 9. She is 'old-fashioned' in her expression and behaviour. There is great enlargement of the ends of the long bones, and a severe condition of knock-knee. Weight 4 st. 11 lb. The temperature chart shows slight daily excursions above the normal.

On a Schmidt's diet the stools showed no excess of roast fibres and no fat globules, but some excess of soap crystals. On an ordinary full diet a loose stool was passed which showed a few fatty globules, and some excess of soap crystals.

Dr. J. H. Ryffel reported quantitatively on the dried faeces and blood-calcium as follows:

Total fatty acid and fat	20·54 per cent.
Fatty acid as soaps	15·62 „
Free fatty acid and neutral fat . . .	13·92 „

These figures are distinctly high but bear normal relationships.

'The serum-calcium was definitely though slightly low as regards total calcium and more so for precipitable calcium.

Calcium in ash of serum, 8·9 mg. per 100 c.c. (Normal 9·2–10·0).

Calcium precipitated directly by oxalate, 7·9 mg. per 100 c.c. (Normal 0·3–0·5 less than Ca. in ash.)'

'Radiograms of the chest showed considerable enlargement of root shadows and shadows in the right upper lobe suggestive of phthisis.' (Mr. P. J. Briggs.)

A fat-free diet was prescribed and, in view of a low curve of gastric acidity, dilute hydrochloric acid m. xxx three times a day with meals. Ten months later the patient's doctor (Dr. C. Ewbank Lansdown) reported: 'Up to present date she has steadily improved on the treatment recommended. . . . There have been only two or three slight set-backs. There has been no return of the grey slaty-coloured motions. She has gained 1 st. 8 lb. in weight. The rickets have to all intents and purposes disappeared. Muscular development has very much improved. She is not like the same child, being happy and cheerful and developing.'

It is not easy to collect information as to the comparative frequency of pancreatic disease and disease of the absorbent

an inflammatory occlusion of some part of the lacteal system is responsible for the common symptoms in these diseases.

4. Whether for combating the main or subsidiary symptoms rigid fat restriction should play an important part in the treatment of such conditions so long as the stools continue to give an indication of mal-absorption of fat.

I am greatly indebted to Sir Arthur Hurst for permission to report upon the three cases referred to above.

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XI

OBSERVATIONS ON COLONIC PAIN[1]

The experimental study of pain in man, if we except certain superficial forms of pain, is clearly limited in its scope, and it is no matter for comment that the subject of abdominal pain has received a somewhat scant attention in the departments of physiology. Balloons and instruments may, it is true, be inserted into the stomach, the gullet, and the rectum, and the effects and accompaniments of certain stimuli have in this way been noted or graphically recorded. But there are many organs and structures inaccessible to such methods of inquiry. Furthermore, it has not been found possible to reproduce, even in accessible organs, the many varieties and degrees of pain naturally peculiar to them, varieties and degrees which must have a physiological, as they undoubtedly have their special clinical, significance. The study of visceral and corporeal pains, ill suited to the method of experiment, has therefore devolved largely upon the physician and the surgeon, who, employing the method of observation, must endeavour to gather and piece together those links in the chain of evidence which the physiologist at present seeks in vain.

But if the experimentalist is hindered by his lack of opportunity and material, the clinical observer is often overwhelmed by the wealth of his, and is further hampered by the difficulty of imparting accuracy to his observations. Intelligence and precision are commonly lacking in the patients upon whom Nature performs before him her experiments in pain, and temperamental peculiarities render the assessment of pains most difficult. Moreover, the problem of accurate diagnosis is ever present, and for the study of pain due to a particular lesion we need not only to know the nature of the lesion and its situation, but also its extent, the tissues involved, and the character of any associated derangements of function. It may be said that in the case of

[1] *Guy's Hosp. Reports*, 1920, lxxix. 295.

painful, malignant, and inflammatory diseases never, and in painful mechanical disorders seldom, does Nature provide us with a 'clean' experiment. When she produces visceral pain in the absence of a lesion the seat of the pain is commonly invisible and impalpable, and if the organ is accessible to radiological or other instrumental survey, it may happen that the pain is in abeyance at the time of the investigation.

It is therefore pertinent to ask whether there exists any disorder commonly encountered in medical practice in which, without demonstrable organic disease, a pain occurs which is true to type, and with which there are objective associations also true to type and of such a kind as to suggest both the seat of origin of the pain and its essential cause. A near approach to these conditions obtains in the case of a disorder, not extremely rare, a cause of chronic or recurring abdominal pain, and one deserving of recognition if only because it leads too frequently to operations for supposed organic disease. This disorder has been variously described as spastic constipation, chronic colo-spasm, tonic hardening of the colon, and spastic colon. Certain observations on the pain which is the leading symptom of spastic colon (I use the term for convenience) may, I think, be appropriately reported here. Descriptions of the malady have been furnished at various times by Howship [1], Cherchewsky [2], Fleiner [3], Hawkins [4], Hurst [5], and Turner [6]. Stacey Wilson [7] has devoted a book to the subject, and I have myself redrawn the clinical picture in some detail.[1] I have also described elsewhere a simple system of interrogation which has seemed to me useful in the prosecution of any clinical inquiry into pain.[2] The ten questions included in this interrogatory and the usual answers to them given by sufferers from spastic colon may be briefly recounted.

The first two questions are concerned with (1) the *character* and (2) the *degree* of the pain. Three questions have a bearing on spatial relationships and are answerable under the headings of (3) *situation* (including depth from the surface), (4) *localization* (or extent of diffusion), and (5) *paths of*

[1] See Lecture XII.

[2] See Lecture III.

reference. Three questions have a bearing on temporal relationships and are answerable under the headings of (6) *duration*, (7) *frequency*, and (8) *special times of occurrence* or *non-occurrence*. The two remaining questions are answerable under the headings of (9) *aggravating* and (10) *relieving factors*. Finally, it is necessary also to review *associated symptoms* as indicating contemporary disturbance of function.

The *character* of the pain in spastic colon is usually a 'dull, steady ache', sometimes 'gnawing', and never griping as is the peristaltic pain of purgation or obstruction. It is usually quite 'bearable', although 'tiring' and 'worrying'. Occasionally, however, it is of very great severity and may even simulate the major 'colics' and require morphine for its relief. Its *situation* is in the course of the ascending, the descending, or the transverse portions of the colon, in this order of frequency, or in two or all three of these situations. Sometimes there is associated rectal pain. The *localization* corresponds with the surface marking of the colon and the descriptive gestures may be remarkably precise. The patient in whose case the appearances shown in Figs. 1 and 2 were noted surprised her radiologist by accurately demonstrating to him the course of her transverse colon on the basis of her sensations. Sometimes there is a diffuse lower abdominal reference, but more commonly the palm of the right or left hand applied to the corresponding iliac fossa or the ulnar border of the hand drawn horizontally across the abdomen indicates the site and the narrow linear distribution of the pain. I have not convinced myself of the occurrence of *referred* somatic pain or *tenderness* in spastic colon. The pain is felt internally and has no segmental distribution. These observations support the contention, based also upon *observations in other abdominal diseases*, that *referred* somatic pain and tenderness express either a strong sustained type of stimulus such as inflammation or ulceration or, more rarely, an extremely severe *mechanical stress* such as obtains during the passage of a calculus, while they are usually absent or inconspicuous in painful visceral disorders of other causation. The *duration* of the pain is given in

terms of an hour or hours or even days, not in seconds or minutes as in the case of peristaltic pain. Its frequency is variable, and depends much upon the circumstances of the patient's life and general health. A *special time of occurrence* is two or three hours after food, and of *non-occurrence* during the night, when, with warmth and physical and mental relaxation, the pain departs and good sleep is generally enjoyed. Of *aggravating factors*, cold, fatigue, worry, jolting, exercise, purgation, and tobacco are the most important. Of *relieving factors*, warmth, holidays, belladonna, and large warm enemata are noteworthy examples. *Associated symptoms* include constipation frequently, diarrhoea less frequently, and intestinal flatulence. Gastric pain, urinary frequency, dysmenorrhoea, and vascular spasm as shown by the symptom of 'dead fingers' are also common and proclaim the general irritability of plain muscle which characterizes these cases.

The chief objective association is a palpable hardening of the affected portion of the colon, which may be felt through the abdominal wall as a firm rod or sausage-like tumour. This sign depends upon tonic rigidity, shortening and straightening of the affected loop. The same phenomenon may sometimes be witnessed in the course of an abdominal operation when a loop becomes hard and pale and rigid in the wound through tonic contraction. At the bedside the degree of hardening may be felt to vary under the palpating hand, and I have known the pain to become more severe when the hardening is extreme and to disappear with the 'fading' of the 'lump'. Often tender when contracted, the bowel is less so, or not at all, when relaxed. Sometimes this tonic contraction extends to the rectum, and what Stacey Wilson [7] has aptly likened to a cartilaginous ring may be felt on digital examination. Sustained ring contraction may be observed during the routine performance of sigmoidoscopies, but in my experience it is more pronounced and frequent in sufferers from spastic colon. When the lumen closes to a pin-hole in front of the advancing tube, the patient may grunt and groan and complain of lower abdominal or rectal pain. The mucosa is normal in appear-

coat or to the diminished vascularity which accompanies extreme muscular contraction (muscular ischaemia from arterial constriction is now held to be the cause of pain in angina pectoris and angina cruris), or to some other cause, we cannot at present say. Kinsella [8], discussing the pain of gastric ulcer, protests that too much stress has been laid upon the muscular elements in the production of gastric pain, and that the local effects of inflammation have been neglected. He appears to have overlooked the fact that gastric pain, closely similar to and as severe as the pain of gastric and duodenal ulcer, can occur in the absence of a gastric or duodenal lesion. I would submit that we have also in the pain of spastic colon a clear example of a 'gnawing' or 'aching' visceral pain, sometimes very severe, which occurs in the absence of any lesion of the serous, mucous, or muscular coats, but demonstrably in concert with sustained contraction of an abnormal degree. Clinical studies indicate that this behaviour of the colon depends in part upon an inherent neuro-muscular irritability akin to that which is held responsible for the bronchial spasm of asthma. Like asthma, it is associated with particular constitutional types. The two conditions may occur in the same individual or the same family.

The pain of spastic colon is sufficiently troublesome and persistent to lead to diagnoses of appendicitis, gall-stones, renal stone, ulcer, and new growth. By its character and associations alone it can frequently be distinguished from the pains due to these causes. Its differentiation is practically important both for the avoidance of unnecessary surgical procedures and as a basis for appropriate medical treatment.

Summary

Observations on colonic pain have been reported as contributory to the consideration of abdominal pain as a whole, and in support of the thesis that the pain of disease affecting a hollow viscus is experienced in the viscus and is a function of its musculature; that visceral pain may be localized with considerable accuracy; that, where inflammation or severe

mechanical stress is lacking, referred somatic signs and symptoms are generally absent; and that the pain of organic visceral disease, in itself evidence of a functional disturbance, may be closely simulated by the pain of a functional disturbance without organic disease. It is not suggested that an abnormal degree of tonic shortening or hardening is the sole cause of pain in the hollow organs of the abdomen, for there are other stresses, not considered here, whereby tension in plain muscle-fibres may be exaggerated with resultant pain.

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XII

CHRONIC SPASMODIC AFFECTIONS OF THE COLON AND THE DISEASES WHICH THEY SIMULATE[1]

Of the problems which confront the physician and the surgeon few are more troublesome than those which require the interpretation of chronic or recurring abdominal pain. Frequently the diagnosis must be attempted in the absence of any conspicuous objective sign, and, with symptoms for guidance, a decision must be made between 'organic' and 'functional', or, what is more serious for the patient and more exacting in clinical judgement, between a surgical and medical plan of relief. Modern investigations do not always provide the clue. Discussions which serve, in however small a degree, to illuminate this dark field of diagnosis are therefore to be encouraged, and we should be very ready to share our observations and our difficulties.

However great the triumphs of surgery may be in the acute abdominal catastrophes and in certain forms of chronic abdominal disease, none of us can feel content with the present position of abdominal surgery as a whole. We still see too many scarred abdomens with persistence of symptoms, too many 're-operations' and operations undertaken for pain, and it is disturbing to reflect upon the hours which must be lost annually to surgeons and their patients in the conduct of unrewarded appendicectomies, a considerable proportion of which have doubtless been advised by physicians. I would suggest that our shortcomings are less in respect of technique than of diagnosis, employing the term in its fullest sense of 'thorough knowledge' of our cases.

Such remarks as I shall have to make are to be regarded as a slender contribution to the study of a not uncommon abdominal disorder which is characterized by frequent and prolonged discomfort, or troublesome and even severe pain; which is unassociated with any demonstrable organic change in the abdominal viscera; which sometimes simulates impor-

[1] *Lancet*, 1928, ii. 1115.

tant organic disease; and for which consequently operations and explorations are performed.

The condition is variously referred to in the literature as *spastic constipation*, *chronic colospasm*, *spastic colon*, and *tonic hardening of the colon*. For convenience I shall refer to it as *spastic colon*.

Historical

In Chapter IV of his *Constipation and Allied Intestinal Disorders* Hurst [1] gives a useful bibliography of the subject and a concise account of the aetiology and important clinical features of the malady. It was first described by John Howship [2], surgeon to St. George's Infirmary, London, in 1830, in a small and very readable book entitled *Practical Remarks on the Discrimination and Successful Treatment of Spasmodic Stricture in the Colon considered as an occasional cause of Habitual Confinement of the Bowels*. He recognized that the complaint was due to 'a deficient freedom of relaxation in some part of the intestinal canal', and both as a diagnostic test and a therapeutic measure advocated gradual distension of the bowel with a large warm gruel enema. Cherchewsky [3], who was unfamiliar with this account, redescribed the condition in 1833. Fleiner [4] wrote his first article on spastic constipation in 1898. In this country Hawkins [5] wrote an admirably descriptive paper based on the study of 35 cases of enterospasm in 1906, drawing particular attention to the frequent confusion of the disease with appendicitis. The subject has hitherto attracted more attention on the Continent, but latterly there has been a revival of interest in England. Turner [6], from the surgeon's point of view, furnished an article to the *Guy's Hospital Reports* in 1924. Dr. G. Evans made it the subject of a communication to the Association of Physicians of Great Britain and Ireland in 1928. Stacey Wilson [7, 8], who had previously discussed the physiology of the pain in this disorder, has summarized his own views and wide experience in a book entitled *Tonic Hardening of the Colon*. In this he discusses clinical features and advances his own therapeutic beliefs, but attributes, in my opinion, too long

a list of physical nnd mental disturbances to the direct agency of tonic hardening.

The Clinical Picture of Spastic Colon

The descriptions which follow are based on an nnalysis of 50 cases interrogated nnd examined by myself. The series includes 39 cases of spastic colon unaccompanied by an excess of mucus in the stools and 11 cases of the condition usually called muco-membranous colitis, or, better, mucous colic or muco-membranous colic, for cytological examination of the stools and the sigmoidoscope reveal no signs of ulceration and little or no evidence of active inflammation of the mucosa. The cases were taken from my files consecutively and with no special selection, excepting that those in which there was an element of doubt or obvious coincidental disease were excluded. The proportion of 'spastic colon' cases to cases of '*mucous colic*' *is, I believe,* representative. The more detailed consideration of netiology, symptoms, and physical signs is preceded by an account of an individual case portraying the more important features.

Case 1. A middle-aged professional man, of lean type and nervous constitution and liable to migraine, first started to have right-sided abdominal pain some 16 years ago. At one time and another, cholecystitis and appendicitis were diagnosed, and finally, after careful investigation, the appendix was removed. He still, however, has the right-sided pain, and at times can feel for himself a sausage-like lump in the right flank. The attacks arrive especially in spring and autumn, and are precipitated by cold, fatigue, and mental worry. In a hot bath the pain is eased and the tumour fades away. The patient and his brother are both unable to face a cold east wind without developing abdominal pain. The pain shows a tendency to appear 2½ hours after a meal. Examination revealed general right-sided tenderness, and on one occasion the caecum or ascending colon became vaguely palpable. The descending colon was felt like a firm cord, and occasionally the transverse colon was also felt. There were no other signs of disease. The patient found that a good open-air holiday with exercise and mental rest was best calculated to bring relief. At a later date he developed a duodenal ulcer.

Aetiology of Spastic Colon

Sex Incidence.—In the present series of 50 cases there were 17 males and 33 females. Excluding the cases with

mucous colic which, with rare exceptions, are confined to the female sex, there were 16 males and 23 females.

Age Incidence.—The youngest patient was aged 19, the oldest 78. The average age was 39.

Physical and Psychological Types.—Nineteen cases were specifically described in my notes as 'lean', 'thin', or 'spare'. 'Wiry', 'dark', 'tall', and 'pale' were other adjectives which occurred with conspicuous frequency. Twenty-seven cases were recorded as nervous, neurotic, worrying, or anxious. Migraine and asthma were entered against the patient or an immediate relative with sufficient frequency to suggest a more than coincidental association. The association with asthma is commented upon by Hawkins [5].

Family History.—In addition to these associations and general references to 'nervous stock' there were two examples in my series of two brothers both suffering from spastic colon.

The evidence for a constitutional or diathetic factor is thus fairly strong, and has, I think, usually been remarked by those interested in the condition. Conversely I would suggest that it is extremely rare to meet with spastic colon in fair-haired, blue-eyed, healthy-complexioned types with placid dispositions or in robust individuals. In my own experience spastic colon is more common in private than in hospital practice. As Hawkins remarks, 'Intestinal neuroses diminish in frequency as we descend the social scale.'

Predisposing Illnesses and Intoxications.—*Dysentery*, as might be expected from the habit of irritability which it engenders in the bowel, may be followed by spastic colon, and this even for years after the active infection has subsided. Three cases occurred in my series. Hurst also refers to the influence of lead and tobacco, and to colonic spasm reflexly induced by gall-stones, ureteric calculus, or other irritative visceral lesions, or due to tabes dorsalis. It is very difficult to assess the part played by *tobacco*. I would suggest that it is rarely the sole or main factor. Most of my male patients were smokers, and four of them really excessive smokers. On the other hand, the majority of the women

were non-smokers. Occasionally I have seen patients with spastic colon in association with other manifestations of tobacco excess, such as sweating, dizziness, and palpitation. Plumbism and such coincidental diseases as appendicitis, diverticulitis, gall-stones, and tabes were, so far as possible, excluded. The causal or contributory *effect* of *purgatives* must be given due prominence. Thirty of the cases were recorded as constipated, and of these the majority were taking laxatives or purgatives occasionally or habitually. It cannot be doubted that undue irritability of the neuro-muscular mechanism of the bowel is present in these cases, and that the majority of the popular purgatives, however mildly so, are irritants. Furthermore, not a few of the patients are well aware that their pain may be aggravated by purgation.

Constipation.—How far constipation is to be regarded as a cause or a consequence of the spasm it is difficult to say, but, as already mentioned, it was present in 30 (60 per cent.) of the cases. Nevertheless it is important to recognize that pain and tonic hardening of the colon are consistent with *regular* and apparently *normal* bowel *function*. Attacks of 'diarrhoea' are a constant feature in mucous colic. Diarrhoea, occasional or constant, was also recorded in 7 cases of simple spastic colon. In some cases, both costive and otherwise, it is tempting to believe that a low-grade colonic infection is at work, but we have no certain information on this point. The cases are not pyrexial.

Frequency of Previous Appendicectomy

In 18 (36 per cent.) of my cases the appendix had been removed. In one of these it was removed during a laparotomy which I myself advised (*vide* Case 3). In only three instances was it specifically noted that the appendicectomy was undertaken for acute appendicitis. In several instances the operation was undertaken for relief of pain not dissimilar from that for which relief was again sought. In one case there had been two further explorations. In other cases a diagnosis of 'chronic appendicitis' had been suggested.

The Patient's Symptoms

The leading complaint is usually of discomfort or pain in the lower abdomen. The *discomforts* are variously described as a feeling of stagnation or 'stoppage', as 'a ball' or 'a lump', or as a sensation 'like a bar of lead'; the direction of this bar may actually correspond with some part of the large bowel, and the description is remarkable for the nicety with which it interprets the tonic rigidity present in the affected segment. The *pain* is usually a dull continuous ache, sometimes 'gnawing' or 'like a toothache', never rhythmical or griping as in the colic of purgation, acute enteritis, or intestinal obstruction, and even in the severe cases unlike the sharper, immobilizing pain of an acute inflammatory lesion. It varies in severity from something quite trivial to an intensity—as will be described later—so severe as to simulate the major colic of a ureteric calculus, and to call for the administration of morphine. These severe cases are fortunately rare. Diagnosis even in the attack may be extremely difficult. In a case of average severity the pain is at times troublesome enough to interfere seriously with work or pleasure, although it is noteworthy that sleep is seldom lost on account of it. It is usually referred with accuracy to the part of the colon involved, and I must differ from Stacey Wilson [7, 8] when he states that the distribution is segmental. A common gesture is the application of the palm of the right or left hand to the corresponding iliac fossa, when the proximal or distal portions are affected. In the case of the transverse colon the course of the pain is traced with a finger or shown with the ulnar border of the hand. For purposes of brevity I tabulated the caecum and ascending colon as 'first part'; the transverse colon as 'second part'; and the colon from the splenic flexure to the commencement of the rectum as 'third part'. Of the cases in which observations of the part affected were noted the first part was indicated in 26, the second in 14, and the third in 21. Rectal pain was also recorded in a few cases. Some patients could only describe a vague lower abdominal 'stomach-ache'. Variations in the situation of the pain are spontaneously

described. Associated pyloric spasm and, in women, bladder discomfort and frequency are not rare. 'Dead fingers' are a common complaint. With the pain there is often mental depression or irritability and physical inertia. Both onset and relief may be abrupt and occur for no apparent reason. The duration of the pain varies from an hour or less to many hours or even days.

Of aggravating or precipitating factors I would particularly mention cold and fatigue, each of which was specifically recorded in 14 instances; jolting, such as results from games or digging, horse-riding or motoring over rough roads, and even walking; mental stress or worry; purgatives; tobacco; and, in women, the menstrual cycle. The more irritable cases of mucous colic are very susceptible to fruit. Patients are sometimes more, sometimes less, comfortable when their bowels are confined, but aggravation of pain immediately after the act of defaecation is common. Warmth, rest, hot baths, and open-air holidays with freedom from cares are among the relieving factors. Food sometimes gives temporary relief.

Physical Findings

To these disturbed sensations certain objective information can be added in a high proportion of cases, more especially if the opportunities for examination are frequent. The physical sign of the disease is an unusual palpability of some part or parts of the colon; this depends upon tonic rigidity, shortening and straightening of the affected loop. The colon can often be felt in the left iliac fossa in healthy persons or in patients without colonic disease, and simple palpability in this region cannot be regarded as pathological. In spastic colon it is felt as an unduly hard cord of small calibre. It is doubtful if the colon is ever palpable in its proximal or transverse portions in perfect health. In the condition of spastic colon, however, either of these portions may be felt as a firm rod or sausage-like tumour. This is sometimes, but by no means always, tender. The degree of palpability varies from time to time, and even in the course of a single examination, and is more likely to be remarked

when symptoms are present. In those cases in which undue palpability was noted in my series the first part was affected in 18 instances, the second part in 8, the third part in 9. The first and third parts were simultaneously felt in 3, and all three parts in 4 cases. What Stacey Wilson aptly likens to a 'cartilaginous ring' may sometimes be felt on inserting the finger into the rectum. Occasionally attacks of ballooning of the caecum are observed behind a spastic ascending colon.

The stools as a rule show nothing very characteristic excepting in the group to be separately considered under the heading of mucous colic. In the larger group there is no mucous excess or occasional very slight excess; no blood; and the colour varies within normal limits. There may, however, be fragmentation, and, in the presence of anal spasm, narrowing of the faecal mass. If purgatives are being used the motions may, of course, be 'loose', 'messy', and unsatisfactory.

Sigmoidoscopy is often both difficult and painful on account of spastic narrowing of the rectal and sigmoid lumen which is further stimulated by passage of the instrument. Fluctuations in the degree of spasm can be witnessed simultaneously with variations in the pain complained of by the patient. The mucosa looks perfectly healthy.

Less is to be gleaned from *X-ray examination* than might be supposed. In the first place, the spastic state is intermittent and may not coincide with the examination. In the second place, a barium enema, which is commonly used in preference to the barium meal in colonic cases, may, by its gradual introduction and gentle distension, overcome existing spasm, just as Howship was able to overcome painful spasm with a large gruel enema; in the third place, when views are taken after evacuation of the bulk of the meal or enema, it is necessary to distinguish the appearances of a normal but partly emptied segment from a segment with spastic narrowing of its lumen. Examination after a barium meal is more likely to give positive evidence. In extreme cases the affected length of bowel appears as a thin thread

or streak of barium, sometimes with a sharp line of demarcation from the better filled portions. Normal haustrations, deepened with lesser degrees of spasm, become obliterated when the spasm is very pronounced. In some cases the whole transverse or descending colon or a longer portion is involved; in others, but less frequently, the spasm is localized to an inch or two. The localized spasms cause a more intense pain. Two other departures from the normal are important and will be discussed later. These are shortening and straightening of the affected loop.

Mucous or Muco-membranous Colic

(*Muco-membranous Colitis*)

I see no valid reason for placing these cases in a separate category. The abdominal pains described, the aggravating and relieving factors and the radiographic appearances are identical. The chief differences are as follows: (1) the sex incidence, the cases being almost all in women; (2) the passage in attacks (usually after a period of constipation, chilling, anxiety, or fatigue) of large quantities of coagulated mucus, sometimes in casts or shreds or enveloping small scybalous fragments; (3) the more evident neurotic associations; (4) an exaggerated colonic tenderness with flinching and hyperalgesia, but less definite palpability of the bowel. The sigmoidoscopic findings are as described in simple spastic colon. The mucosa is smooth, and, at the most, slightly redder than normal.

Differential Diagnosis

Judging by my own difficulties and those experienced by colleagues who have referred cases to me, the following conditions are among those which are simulated or suggested by the 'spastic colon': (1) appendicitis, acute and chronic, (2) duodenal ulcer, (3) diverticulitis, (4) colonic carcinoma, (5) renal colic, (6) intestinal obstruction, (7) ovarian or tubal disease, (8) neurasthenia and hypochondriasis, (9) faecal tumours. Finally (10) the cases with mucous excess seem not infrequently to conjure doubts

about the possibility of ulcerative colitis, or have been vaguely classified as 'colitis'.

(1) *Appendicitis.* In one of my cases the hard lump in the right iliac fossa formed by the contracted colon during an attack of pain had led a surgeon to a provisional diagnosis of appendicular abscess. More usually the persistence of symptoms leads to appendicectomy for a so-called 'grumbling appendix'. In simple spastic colon there is, as a rule, no pyrexia, guarding, vomiting, or cutaneous hyperalgesia. In acute exacerbations of mucous colic there may, however, be slight pyrexia, flinching (rather than guarding), superficial soreness, deep tenderness, and even sickness; but the previous history, the patient's psychology, and inspection of the stools generally establish the diagnosis. In simple spastic colon the interrogation, particularly in regard to the nature, duration, and localization of the pain, and careful palpation along the course of the colon are usually adequate. (2) *Duodenal ulcer* may be simulated, firstly, because of associated pyloric or gastric spasm with food relief; and, secondly, because the colonic pain itself, although differently situated, may develop late after meals and be relieved by food. The two conditions may also occur together. If there is any suspicion of duodenal ulcer as an alternative or additional diagnosis a full investigation should be advised. (3) *Diverticulitis.* In the left-sided cases particularly this possibility must be borne in mind, but the type of individual affected is usually different, the victim of diverticulitis being commonly well nourished and less commonly neuropathic. The inflammatory tenderness and thickening of pericolitis and pyrexia during exacerbations are distinctive. X-ray examination after a barium enema should be made in case of doubt. (4) *Colonic carcinoma* has frequently been feared in cases of spastic colon because the patient himself or his physician has discovered a hard lump in the course of the colon. The smoothness of the tumour, its sausage- or rod-like formation, its mobility in the case of the ascending or transverse colon, its variations in size and hardness, or complete disappearance under observation or in a hot bath are helpful points in differentiation. The

absence of obstructive symptoms on the one hand, and of diarrhoea or passage of blood on the other, and generally a very long history of abdominal discomforts are reassuring features. If doubts persist the aid of the radiologist, sigmoidoscopy, and chemical and cytological examination of the stools should be invoked. (5) *Renal colic* is only likely to be simulated in the occasional cases with very severe pain (*vide* Case 3, in which the hardened colon was mistaken by myself and others for the left kidney). (6) *Intestinal obstruction* was feared in Case 4, in which the complication of caecal distension was present. (7) *Ovarian or tubal disease.* At one time it was not uncommon for operations on one or both ovaries, but especially the left, to be performed for spastic colon. The fallacy probably arose from the aggravation of colonic pain which sometimes accompanies the period and from the association with dysmenorrhoea. (8) *Neurasthenia* and *hypochondriasis* may appear appropriate labels in some cases of spastic colon, but they do not embody an adequate explanation of the pain and physical findings. (9) *Faecal accumulations* can be disposed of with enemata. (10) '*Colitis*' is an inaccurate pathology. I have had several cases of mucous colic referred to me with a diagnosis of *ulcerative colitis*, but the two conditions bear little resemblance to one another. In the more serious disease an ill and frequently anaemic and wasted patient gives a history of watery diarrhoea and passing blood and mucus, commonly with a febrile, dysenteric onset. The diagnosis is completed with the sigmoidoscope.

Frequency of Spastic Colon

Taking all grades of the condition, allowing for its varied appellations and deceptions, and judging by information received from colleagues in general practice, I can only conclude that spastic colon is a common disorder. On the basis of consulting and hospital experience I should say that it ranks high among the causes of chronic abdominal distress. Numerically in my index it is more frequent than gastric ulcer, but less frequent than duodenal ulcer, conditions which are far more likely to be referred for a second opinion.

Nature of the Disorder

'Spastic colon' falls into the category of the visceral neuroses. Its association with certain physical and psychological types; its intermittent behaviour; its aggravation by circumstances which depress or harass the higher centres, and the absence of all evidence of an associated organic lesion, give credence to this view. It is a close ally to bronchial asthma, in which an inherited irritability of the bronchial centres and a sensitiveness to certain local, psychic, and peripheral stimuli are, on Hurst's [9] showing, so apparent. Just as with asthma, so with spastic colon, cases occur in which spasm alone is the outstanding feature, and others in which mucorrhoea is superadded. Asthma is sometimes coincident with colonic spasm in the same patient or recorded in a near relative. The stimuli which may provoke and perpetuate an attack of colonic spasm include (1) local stimuli (coarse foods, purgatives, constipation), (2) central nervous stimuli (worry), (3) external peripheral stimuli (cold). The same irritability of plain muscle is often simultaneously manifest as bladder frequency and even bladder pain, especially in female sufferers from spastic colon; in pyloric spasm; spasmodic dysmenorrhoea; and in the vascular spasm which gives rise to 'dead fingers'.

Nature of the Spasm and Pain

In obstructive or irritative lesions of the colon there is increased peristaltic activity with more or less rhythmical griping due to the passage of waves of contraction involving successive groups of circular fibres. In spastic colon no such rhythmical movements are provoked, but the tonus or posture of the muscle-fibres, including the longitudinal fibres, is modified in such a way as to impart a sustained shortening, with rigidity and narrowing of the lumen, to portions of the bowel wall often many inches in extent. The hardness and equally the straightening and shortening of the affected loop cannot be otherwise explained. I was at one time puzzled by finding a hardened and horizontal transverse colon crossing the epigastrium, for although this

is its anatomical situation I knew that the radiologist more frequently showed this structure as a festoon in the middle or lower abdominal planes and sometimes even in the true pelvis. Surgeons sometimes witness the phenomenon of tonic hardening in the course of a laparotomy when the affected loop becomes rigid, pale, and erect in the wound. I know no clinical condition which better supports the hypothesis that visceral pain originates in the viscus and is due to increased tension in the muscle-fibre than spastic colon. With no inflammatory disease to involve the other coats of the bowel or neighbouring tissues, and so to confuse the issue, it is possible to demonstrate in these cases at once a complete absence of somatic hyperalgesia and well-defined pain and tenderness in the affected bowel itself, a pain and tenderness which increase when the hardening increases and diminish when it diminishes. The sustained and aching character of the pain accords well with this durable modification of tonus or posture, and contrasts with the sharper, transient agony of peristaltic colic.

Illustrative Cases

Case 2. *Illustrating the influence of cold, the simulation of appendicitis, and the cause of the pain.*—A young and athletic lady, aged 25, developed pain in the right iliac fossa on a long voyage. The ship's doctor diagnosed appendicitis, but would not operate on board. On arrival in England her own medical adviser and a surgeon saw her and concurred in the diagnosis, but freely admitted that the appendix when removed was 'disappointing'. The other organs were healthy. The pains recurred and she was brought to see me. I obtained an earlier history of *many attacks of sudden and intensely severe pain coming on ten minutes after a long swim*, in which she was doubled up, looked green and ill, but was relieved by brandy. Since the operation there had been a slight looseness of the bowels. She had noticed aggravation by fatigue, cold, and by fruit and green vegetables. During my examination I was able to demonstrate a hardening of the colon in the right iliac fossa which came and went, the pain coming with the 'lump' and disappearing as it 'faded'. The diagnosis had been made easier for me by the negative operation findings, but the earlier history of precipitation by cold was instructive.

Case 3. *Illustrating difficulties in differential diagnosis, the occasional severity of the pain, and aggravation by an enema, jolting, &c.*—An infantry officer, aged 41, consulted me on 25 February 1926 for

severe pain in the left subcostal region passing through to the back at the same level. He had also felt the pain in the mid-epigastrium where he had been tender. He had suffered similar symptoms a year and also 5 months previously, but less severely. The pain was liable to come one or two hours after food, and was sometimes relieved by eating. Jolting definitely aggravated it. His actual sensations he likened to 'a lump of dough stuck and swelling as though about to burst'. He was lean, tense and tremulous, and very tender in mid-epigastrium. I made a provisional diagnosis of gastric ulcer and put him into a nursing home for observation. On 27 February he had a very severe attack of pain below the left rib margin and radiating down towards the groin. *The pain immediately followed an enema.* Morphine was given on more than one occasion. He was tender under the left ribs and I queried feeling the kidney. Jarring the loin also caused pain. Urine normal. His wife then remembered that for years he had had an occasional day in bed for left-sided pain. While I was away for a week-end, the patient, my deputy, and the nurses all noted the presence of a lump below the ribs which was gone on my return. I now decided to regard the symptoms as renal. A surgical colleague who saw him with me concurred, but cystoscopy and pyelography were negative. The pain continued, and he was explored on 14 March, all investigations having proved negative and all medical treatment unavailing. A slightly fibrotic appendix was removed, and adhesions between the duodenum and gall-bladder were freed. No ulcer, gall-stones, growth, or other abnormality were demonstrable. He was not relieved of his symptoms by the operation, although reassured in his mind by the findings. I was then able to satisfy myself that both the pain and the lump were colonic and due to tonic contraction. I have seen only a few other cases in which the pain was so severe and none so deceptive in their symptomatic associations. I saw this patient, who remains on duty, later, and was able to feel the hardened colon to the left of the navel. He is quite sure that jolting and cold, which I had come in the interval to recognize in other cases as important aggravating factors, are very definitely so in his case. I should clearly have paid more attention in his first bad attack to the influence of the enema.

CASE 4. *Illustrating the severity of symptoms, ballooning of the caecum the shortening and straightening of the colon, and the accuracy of localization by the patient's gesture.*—I was consulted by a woman aged 40. From girlhood she had suffered from constipation and a liability to nausea, and had been prevented by her poor health from taking up work in which she was interested. In 1921 she had acute gangrenous appendicitis. Since then she had, in the words of her medical adviser, had three or four attacks 'almost like partial obstruction'. These start with feelings of pain and weight in the caecal region where a big bulge appears. In her last attack she could 'feel the bowel like a

lump', and was in pain for four or five hours continuously. The pain also passed straight across her abdomen to the left. Lesser attacks were brought on by work in the garden and could be cut short by lying down. There was aggravation by purgatives and her pain was worse *after defaecation*. *On palpation I was able to feel a hardened* colon which again 'faded' under my hand. The radiograms showed an extreme degree of colonic spasm affecting first the transverse and later the descending portion. During the examination she surprised the radiologist by *accurately tracing the course of the transverse colon by her sensations*. This straight course from hepatic to splenic flexure is well shown in the illustrations to Lecture XI. Her brother later consulted me for similar symptoms.

Treatment

Most patients with '*spastic colon*' have been walking in fear of organic disease; many of them have been told that they have organic disease; cancer-phobia is frequently present; operations may have been advised or already performed. The first duty of the physician is therefore full reassurance. With this must be combined a simple explanation of the nature of the disorder and the mode of origin of the pain. Under general hygienic measures the importance of mental and physical relaxation, of holidays, of moderate exercise, of warmth, and a sensible mixed diet must be enumerated. Often the diet has been cut too low and fruit and vegetables have been too rigorously excluded. The bulky starchy foods, potatoes, beans, and peas, which predispose to intestinal flatulence, are better avoided, but fruits of all kinds, excepting those with tough skins and seeds, and the softer green vegetables should be liberally prescribed together with whole-meal bread and farm produce as a natural treatment of the costive tendency. Tobacco may require restriction or even be forbidden for a long test-period. Purgatives must be entirely forbidden, but lubricants may be given. Belladonna in full pharmacopoeial doses helps to relax the spasm. Bromides should be reserved for the anxious and 'jumpy' patients, and withheld in the case of the more jaded and depressed. There is commonly restlessness with a furrowed brow, and hypertonus of skeletal muscles. Psychotherapy plays an important part in the treatment of such cases. Jackson [10] has described a

method of treatment by 'progressive relaxation' in which clinical improvement is shown to coincide with a return to normal in the colonic radiograms and diminution in the briskness of the knee-jerks. The good sleep enjoyed by most patients, even when suffering bad pain by day, is probably due to the relief afforded by natural muscular repose. In some cases the sallow complexion and lassitude and a furred tongue during the attacks seem to suggest an element of what—for want of a more precise term—we must continue to refer to as intestinal toxaemia. I think it must be in these cases especially that Stacey Wilson obtains his successes by exhibiting liquor hydrarg. perchlor. with liquor ferri perchlor. I have not tried his prescription extensively, but in one case it seemed to bring about a remarkable improvement when other remedies had failed and the patient was begging for an exploration. In cases with severe pain and in exacerbations of mucous colic, initial large warm enemata administered very slowly, both to give lavage and to overcome the spasm, and rectal injections of warm liquid paraffin (4 or 5 oz.) to be retained overnight, are useful. The disorder, being like asthma and migraine, so largely dependent on constitutional factors, is difficult to 'cure', but repeated reassurances and rational treatment will often mitigate symptoms even in bad cases. In milder cases there may be complete relief.

Conclusion

I have attempted a somewhat detailed analysis of the clinical picture of spastic colon because the diagnosis of the condition should generally be possible on clinical grounds. Furthermore in functional disorders of this kind special investigations inevitably give a high percentage of negative results. The recognition of spastic colon as an occasional cause of very severe abdominal pain and as a common cause of persisting or recurring pain in the right iliac fossa is, I believe, especially worthy of emphasis. Writing of these visceral neuroses in 1906 Hawkins said, 'They are at this moment particularly worthy of study, owing to the advance of abdominal surgery, not because they are amenable to

surgical treatment, but rather because they need protection.' I think it should be accepted that they still need protection, and that for this and other reasons they are still worthy of study.

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XIII

ON EXAMINING THE RECTUM[1]

THE end of the alimentary passage hides many secrets which are, in more senses than one, fundamental, for diagnosis and appropriate treatment depend upon their timely discovery. There is a saying that the chief clinical advantage of the consultant over the general practitioner lies in his more frequent appreciation of the necessity for a rectal examination. This might seem to suggest errors of omission on the part of colleagues, but it is not a general criticism, and it might equally be taken as a reflection on teaching. All doctors in all branches of the profession—and consultants are no exception—are guilty of omissions from time to time, for they are only human, but the best doctors include those who can claim the fewest omissions in respect of this simple procedure.

I have recently looked through my notes of 14 cases of carcinoma of the rectum. These cases do not usually find their way to the physician; they go to the surgeon, and the majority presumably go with the diagnosis already made. Of these 14 cases, however, 8 had not been diagnosed, notwithstanding that they had had characteristic symptoms for periods varying from three months to four years. Seven had never had the rectum examined. Five had symptoms dating back over a year, and 2 over three years. *The usual diagnosis in unexamined cases was 'colitis'.*

This important procedure is apt to be neglected (1) through lack of appreciation of the indications, and (2) through a natural sense of delicacy in regard to an examination which, in the idea, is so unpleasant and so likely to be repugnant to the patient. Some patients who have to submit to it are, in point of fact, most considerate, and will even express sympathy for the doctor that such a duty should fall to him. Others are squeamish or timid, but if we make a point of being gentle, and are careful to explain

[1] *Guy's Hosp. Gazette*, 1931, xlv. 122.

the value of the examination and how quickly it is over, and to warn them that, while it is likely to be uncomfortable it is only occasionally painful, confidence can soon be won.

A decision to make the examination must obviously be based on history and symptoms. It would clearly be an excess of zeal to make it a part of every routine overhaul. The behaviour of the bowel, abnormalities in the consistence and appearance of the stools, and local pain or discomfort are, of course, the chief indications. If blood is passed it should be particularly noted whether this is with a formed or unformed stool, whether it comes with the stool or separately at the end of it, and so forth. The diseases which we set out to diagnose with the help of the examination are chiefly situated in the ano-rectal canal or its near neighbourhood, but they may also be remotely removed from it.

The Indications for a Rectal Examination

The principal symptoms and occasions which call for the examination are:

1. Pain in the anal or rectal canal; bleeding from the rectum; passage of mucus or pus from the rectum; chronic diarrhoea; obstinate constipation; alternating constipation and diarrhoea; anal pruritus—symptoms, in other words, suggestive of carcinoma, fistula, fissure, piles, proctitis, or colitis. Rectal prolapse or symptoms of intussusception in children are further obvious indications.

2. Urinary symptoms suggesting enlargement of the prostate or pressure upon the bladder or symptoms of disease of the genito-urinary apparatus which might involve the seminal vesicles in the male.

3. Symptoms of uterine, ovarian, or tubal disease in the female and particularly in unmarried women when a vaginal examination is to be avoided.

4. Any suspicion of serious abdominal disease, inflammatory or malignant, in which the possibility of feeling an inflammatory mass (as in appendicitis) or deposits of new growth (as in carcinoma of the stomach or bowel) is entertained.

5. Sciatic or hip pain or other symptoms of possible bony disease involving the sacrum or pelvis, and including osteomyelitis, tubercular trouble, and bony tumours.

6. Rectal spasms, and crises of nervous origin where we must, nevertheless, be at pains to exclude a local cause.

7. Severe unexplained anaemia where malignant disease, a local source of venous or arterial bleeding, or a tarry smear on the tip of the finger-stall may give the answer to our question.

8. Obscure pyrexia in cases where it has become necessary to exclude local inflammatory or malignant causes.

This is a sufficiently long list, but not exhaustive.

The Technique

The anus and rectum may be examined (*a*) with the forefinger, (*b*) with the anal speculum, (*c*) with the proctoscope or sigmoidoscope, and (*d*) by direct inspection during dilatation of the sphincter under an anaesthetic. The most important is the digital method, but more accurate information is often obtained by one of the visual methods. Some teachers, I believe, advise that finger-stalls should not be used, as they diminish tactile accuracy. You should certainly never employ the thicker finger-stalls provided; the finger of an ordinary rubber operating-glove is generally too thick. The thin 'film' finger-stalls, however, now on the market are, to my mind, satisfactory. They are more hygienic than the naked finger, and they afford protection against an occasional, but ever possible, risk of infection. I have never regretted my custom of using one since I examined a case of undiagnosed anal soreness in a young man, who in the following week developed a profuse syphilitic rash. Condylomata are among the most infective of syphilitic lesions.

The Digital Method

For this examination the patient is placed in the left lateral position; the knees should be well drawn up towards the chest, with the buttocks on a level with or just over the edge of the bed or couch. The anal orifice should first be

inspected for external piles or for the surrounding sodden skin of pruritus ani, and then anointed with vaseline. Care should be taken to avoid introducing hair with the finger. Then, if the finger is inserted gently and slowly, discomfort will be reduced to a minimum. The examination may be exceessively painful in the presence of fistula, fissure, a thrombosed pile, a low rectal carcinoma, in cases of faecal impaction, and in certain cases of anal spasm. Otherwise it is usually only uncomfortable. It commonly evokes a sense of the desire to defaecate, and is therefore a cause of mental distress, which can easily be explained away. .

What are the abnormalities which the finger may encounter? Piles, unless they have recently been thrombosed, are soft structures and seldom very evident. An anal fissure, or more correctly an anal ulcer (the impression of a crack or fissure is due to the fact that the ulcer is laterally compressed by the postural tone of the sphincter), may, for all its minuteness, give a very definite impression to the finger-tip, and this is best likened to the feeling of the button-hole on the lapel of one's coat. The track of a small peri-anal fistula or abscess may be felt as a small linear prominence. Direct pressure upon an ulcer or an abscess nearly always evokes instant pain. Ballooning of the rectum gives the impression of a large hollow cavern when the finger has passed beyond the sphincter. By some this is thought to be a sign of obstruction higher up. This is not necessarily so, but it is more common in obstructions or other chronic bowel diseases than in their absence. A carcinoma may be felt as the elevated edge of a hard ulcer over which the finger-tip rides before it drops into a roughened crater, or as an irregular tumour filling the lumen of the bowel. Scybala in a neighbouring loop may easily be mistaken for a tumour or glands. Retained faeces may be present in the rectum as a soft mass or scybalous lumps, or, occasionally, as a large impacted mass capable of causing severe symptoms, as I shall describe.

In certain cases it may be necessary to make a bi-manual examination. It is then wiser to roll the patient on to his back, keeping the finger in position meanwhile, when gentle

pressure on the abdomen may bring a tumour, which could not otherwise be felt, in contact with the finger-tip.

On withdrawing the finger, which should be done slowly and gently, the finger-stall should be inspected for blood or pus, or to observe the colour of adherent faecal matter.

Instrumental Methods

First, we have the anal speculum originally devised by Hilton, which is most useful for inspecting and giving access to an anal ulcer. The instrument explains itself; the removal of the lateral slide gives a clear view of the diseased area.

For the proctoscope and sigmoidoscope we employ the same technique, and they may be considered together. With regard to the preparation of the patient, no purgation should be used. If he is up and about he should be encouraged to have the bowel moved an hour before the examination. If confined to bed, a warm water wash-out should be given early on the morning of the examination, and a later attempt at natural evacuation should be encouraged. A nervous patient may be given a morphine injection 20 minutes before the examination, and if there is anal soreness a cocaine suppository may be inserted. Unless the general condition prohibits it, the examination should be made without an anaesthetic, in the knee-elbow position, with the shoulders low and the buttocks raised and the back well hollowed. Before the instrument is passed a digital examination should be made (1) to afford a reminder of the direction taken by the anal canal and the angle which it forms with the rectum, and (2) because it effects a slight preliminary dilatation before the bigger instrument is inserted. As soon as the instrument has been passed within the rectum the plunger should be removed and the light inserted, and all further progress in its passage should thereafter be guided by sight. The normal landmarks are the two Houston's folds, rather reminiscent, when viewed simultaneously, of the diaphragm of a camera-shutter, and beyond these the pelvi-rectal flexure. As careful an inspection should be made in withdrawing the instrument as in passing

it. Only during withdrawal can we observe the state of the anal canal. The colour and smoothness or otherwise of the rectal mucosa, bleeding on contact with the instrument, or blood, mucus, or pus coming down from above should all be looked for, as well as surface ulcerations or grosser lesions.

Let us now pass to a review of some illustrative cases.

Carcinoma of the Rectum

CASE 1. A woman, aged 58, coming from abroad, stated that she had had an operation for removal of her appendix 4 years previously. The pain for which the operation was performed persisted afterwards. Two years later she had the first of a series of violent attacks of lower abdominal colic. For 18 months she had had continuous abdominal discomfort and pain, and during the past 10 months had frequent calls to stool with passage of blood and mucus. She had lost 3 stone in weight during 4 years, was emaciated and cachectic. She had been treated for 'colitis', and the stools had been examined bacteriologically to exclude dysentery. Rectal examination showed the pelvis filled with a hard mass, and also a hard villous tumour filling the lumen of the bowel. Probably the growth had been there for at least 2 years, and possibly the pain for which the appendicectomy had been performed 4 years previously was the first manifestation.

CASE 2. A woman, aged 61, was sent to me with a diagnosis of mucous colitis. She had been seen by more than one doctor in her own town, had been sent to Leamington for special treatment and was there examined radiologically, and had had Plombières treatment at Harrogate. The duration of her illness was 3 years. The symptoms had started abruptly in the first instance with the passage of blood and mucus, and frequent calls to stool. She had gradually become worse, and her complaint was of violent pain in the lower abdomen and a sensation 'as though her intestine was trying to pass out by the bowel'. Frequency and urgency were so pronounced as to necessitate taking a bed-pan to bed. She had lost over a stone and was thin and anaemic. At the limit of the finger a hard ulcer with a well-defined edge and rough base could be felt.

In such cases, even if rectal examination at an earlier stage failed to make the diagnosis, the symptoms called for a proctoscopic or sigmoidoscopic examination. *Bacteriological and X-ray examinations are clearly quite out of place until the bowel has been examined both digitally and visually.*

Anal Ulcer

CASE 3. A woman, aged 40, was sent into hospital under my care in November 1927 for recurring haemorrhage from the bowel and pro-

found anaemia. The first haemorrhage had been noticed in 1913, and she was treated for bleeding piles. This diagnosis was confirmed by another doctor in 1915. The bleeding would last for a few days, and then recur again after a few months. Gradually the attacks became more frequent. In 1926 she was sigmoidoscoped and a small polyp was removed, but without any effect upon her symptoms. In 1927 the haemorrhages became still more frequent. She became weak and anaemic and complained of shortness of breath. Haemoglobin on admission was 47 per cent. I examined her with the sigmoidoscope on 28 November 1927, passing the instrument 10 in. without difficulty. No abnormality was noted excepting a vascular mucosa in the anal canal. No bleeding occurred at the time. As no cause for the haemorrhage had been forthcoming I examined her again with the sigmoidoscope on 13 December, with a negative result, and then repeated the digital examination and felt a small posterior anal ulcer. Pressure upon this caused distinct pain. On re-interrogation it now became clear that the stools were usually passed separately and that bright blood followed. For the first time the patient admitted also to a 'bearing down' pain after defaecation. She was next examined by Mr. E. C. Hughes under an anaesthetic, when a small posterior anal ulcer with a spouting arteriole in its base was found and cauterized. General advice about keeping the stools soft was given, and the patient's doctor reported in March of the next year that there had been no further bleeding and that the patient felt better than for many years.

Here, then, was a case of intermittent ill health dating from 1913 to 1927, with severe anaemia latterly, due to a lesion so minute that it had several times escaped detection at various hands. A digital examination and a more careful analysis of the symptoms suggested a diagnosis which direct inspection proved.

Here is a second case of anal ulcer but with different symptoms.

Case 4. A woman, aged 33, was sent to me with an 18-months' history of pain, feeling to the patient 'like a fragment of china stuck *somewhere low down' in the left iliac fossa just above the groin*, passing to a similar point in the back and spreading out into the left hip. Her doctor favoured a diagnosis of ureteric calculus. I discovered from her that the pain was aggravated by cold and by jolting in a motor-car, that the bowels were costive, that for a much longer period than 18 months she had frequently passed a little blood at the end of defaecation, and that defaecation had also been painful. I found no evidence of disease until I came to the rectal examination.

This caused undue pain, and revealed a tender point corresponding with a small, roughened area typical of anal ulcer.

Those of you who are not already familiar with them should read in Hilton's *Rest and Pain* his descriptions of cases of anal ulcer with misleading secondary symptoms and referred pains, and particularly the case of the bright young lady in society whose abdomen became swollen, whose character suffered a striking change, who was suspected by one doctor of pregnancy, who became anaemic and endured much distress of body and mind, but whose symptoms were all eventually shown to be due to a small, painful anal ulcer.

If I were to attempt a clinical lecture on 'Minor Maladies with Major Symptoms' I should head the list with anal ulcer.

Ischio-rectal Abscess

I was asked to see a man who had been troubled for three years by the most wearing pain felt over the sacrum, and occasionally radiating along the course of the right sciatic nerve. He had never passed blood, but occasionally there was a little watery discharge after the motion. His doctors had examined the bowel on many occasions, but had found no cause. The sphincter had been stretched twice, with only transient relief. They had been forced to the conclusion that the patient was a neurasthenic, but without feeling satisfied that there was no local physical basis. Close inquiry elicited the fact that the pain, although temporarily easier, was later worse after defaecation. I was lucky, for on rectal examination I found on the right side at the limit of the finger a small linear ridge. Pressure upon this caused pain, and also produced a flow of pus down the side of my finger amounting to half a drachm. It was clear that he had a small peri-anal or ischio-rectal abscess, which underwent spontaneous evacuation from time to time.

Ball-valve Accumulations in the Rectum[1]

Occasionally debilitated patients, and particularly the more elderly, will accumulate large masses of faecal matter

[1] See also Lecture XIV.

in the rectum which they cannot expel. This is especially likely to occur after any kind of dehydration, after a gastric haemorrhage, or after a barium meal.

CASE 5. A woman, aged 72, consulted me on 30 June 1932. From September 1931, when her symptoms started quite abruptly, she had been troubled with great bowel discomfort. There were four or five calls to stool each day, sometimes with a loose result, sometimes with none, and, in the latter event, there was much rectal pain. Mucus had been noticed, but blood on one occasion only. Visits had been made to an institution where 'expert' bowel-lavage was given but without the slightest benefit. The weight had dropped half a stone. The patient was of robust type and well preserved. The only physical finding of importance was on rectal examination, which revealed a large, hard, globular mass of faeces, with a slippery surface, acting as a rectal ball-valve. This mass was later broken up digitally and removed with complete relief of all symptoms.

The return of an enema unaltered does not prove that the rectum is empty.

Anaemia

A young man complained of general symptoms of anaemia which had developed rather rapidly. He had not noticed anything peculiar about his stools, but his appearance and history suggested that the anaemia might be due to bleeding. Rectal examination produced some tarry matter on the finger-stall, and the diagnosis of bleeding duodenal ulcer was established.

Obscure Pyrexia

Here is a case in which I failed to make a rectal examination and so to make a correct diagnosis.

A young man was taken ill with slight sore throat, fever, and malaise. At the time of my visit he had had an evening temperature of 101° to 102° for two nights, and it had now risen to 103°. He felt ill, but complained of nothing localizing. There had been no shivering, but he had sweated profusely. Although his throat was redder than normal there was no tonsillitis, and nothing to be seen to explain his temperature. A routine examination of his systems was negative; the urine was chemically normal; the leucocyte count was 7,800 cells per c.mm. Although I did not think that he had a septicaemia, I took some blood for cultivation. Now here is a point in the history by which I had not been sufficiently impressed. Two months pre-

viously he had gonorrhoea for the second time, but, excepting for a slight morning gleet, he had lost all his symptoms. There was no orchitis. After 3 more days of fever he developed a profuse purulent discharge from the urethra, and the temperature fell. A rectal examination would almost certainly have revealed a prostatic abscess, and would have saved me the trouble of a blood-count and the patient the expense of a blood-culture.

Conclusion

There are certain examinations over and above the routine overhaul of the systems which at times become a positive duty. They are examinations open to all and require no specialist skill. Among them are (1) naked-eye examination of the stools; (2) microscopic examination of the urinary sediments; (3) examination of the fundus oculi; (4) observations on the blood-pressure; (5) estimations of the haemoglobin and inspection of blood-films; (6) examination of the pelvic organs in women; and (7), and last, but by no means least, the humble examination which is the subject of this lecture.

XIV

BALL-VALVE ACCUMULATIONS IN THE RECTUM[1]

THE impaction of hard and bulky faeces in the rectum, particularly in the case of aged and infirm persons, has long been reckoned among the causes of severe constipation. Digital or instrumental fragmentation and removal of the faecal mass is the accepted treatment when enemata are unavailing. Occasionally the mass becomes moulded into the shape of a ball or ovoid, which distends the rectum and, while sufficiently mobile to allow the escape of flatus or fluid material, itself resists all natural efforts at expulsion.

Hurst [1] devotes a chapter of his book on Constipation to this type of disorder, and on p. 258 describes the case of a child aged four who came under his observation with an unusually large colonic accumulation above a movable globular mass weighing a quarter of a pound. He refers to a description of similar accumulations in old subjects by Curling [2] (1876), and accords to Simpson [3] (1849), who specifically employs the term 'ball-valve', the priority for having furnished the first account of the condition. A still earlier account is to be found in the writings of William Heberden [4], who, in a single brief paragraph, aptly depicts the main symptoms and complications as follows: 'The faeces sometimes lie in the rectum for many months, and are collected into a large hard mass, which cannot be voided without the help of a surgeon. The signs of this are, pains in the belly; a constant desire to go to stool, even just after an evacuation; none but liquid faeces are ever voided; and the disorder is attended with a difficulty of making water.'

Many examples of this condition have come to my notice in recent years. These might appear altogether too trivial, and the nature of the symptoms too obvious, to be worth recording, but I am persuaded to do so for the following reasons:

(1) In 6 of 7 cases seen at one period the cause of the

[1] *Guy's Hosp. Reports*, 1928, lxxvi. 175.

symptoms had passed unrecognized by the medical men and nurses in attendance. Three of these cases (Cases 2, 5, and 7) were under close observation in hospital. The seventh patient was a medical man who was able to appreciate the cause of his discomforts.

(2) The direct or complicating symptoms in 5 of the cases were so severe and distressing as to call urgently for relief, and in 3 cases (Cases 3, 4, and 6) had prompted a suspicion of some more serious malady.

(3) In 3 cases (Cases 1, 2, and 7) the trouble was a direct result of an X-ray examination with barium meal or enema, and the accumulation was largely composed of barium sulphate.

In the histories of the first 3 cases there is nothing particularly noteworthy.

CASE 1. A medical man, aged 64, had an obstructive carcinoma of the splenic flexure. He had been examined with a barium enema in order to locate the point of the obstruction. During the ensuing 48 hours he expressed himself as unable to void the 'cement-like' accumulation by natural efforts, and was compelled to relieve himself digitally.

CASE 2. A lady, aged 60, had undergone a routine examination of the alimentary tract after a barium meal. A day or two later she was in great discomfort, and this the nurse had been unable to relieve with enemata. Rectal examination revealed a globular, putty-like mass in the rectum, which could be moved about by the examining finger and which had to be broken up before relief could be obtained.

CASE 3. An old man was sent to my Out-Patients for chronic diarrhoea, and was suspected of having a malignant growth of the bowel. Rectal examination revealed a similar collection of putty-like faeces, *obviously acting as a ball-valve.*

In each of the four remaining cases there were special features which warrant a fuller description.

CASE 4. A marine engineer, aged 30, had been out of employment for two years and often rather short of food. He eventually obtained work on a tramp steamer on which the sanitary conditions were poor, and while on a voyage to Gibraltar experienced pain in the lower abdomen which developed an hour after food. This became worse and worse each day, and at Gibraltar he was put ashore and sent to hospital with a diagnosis of gastric ulcer. He lost his pain after three days on a milk diet and was later invalided home. When I saw him he stated that ever since admission to the hospital he had been

troubled with constipation, defaecation had been very difficult, and he had always felt as if the bowel contained something more to be voided. His weight, which had been 10 st. 7 lb. for years, had fallen to 8 st. The abdomen was everywhere slightly distended and tympanitic, but nowhere tender, and nothing unusual was felt excepting for a resistance rather like a full bladder above the pubes. Rectal examination revealed an enormous faecal accumulation acting as a ball-valve and obviously accounting for his rectal discomforts. The examination caused great pain. A small amount of the accumulation was removed digitally, and immediately afterwards he had the most successful action of his bowels that he had had for weeks. During the next few days the bowel was cleared with the help of enemata and all his symptoms disappeared. He was then admitted to hospital for a routine examination of his alimentary tract. No signs of disease were found. He remained well, and rapidly gained weight.

Case 5. An elderly and obese woman was admitted to Guy's Hospital under my care on account of glycosuria. Shortly after admission she began to complain of pain in the lower abdomen and rectum and developed complete retention of urine. On account of this latter symptom I was asked by my House Physician to see her. Catheterization had then been necessary for 24 hours. I suspected a rectal accumulation, and examination revealed a globular mass acting as a ball-valve. The examination was very painful. The mass was broken up under an anaesthetic and the pain and retention were relieved.

Case 6. I was called to see a case in consultation with the following history: The patient was a woman, aged 60. She had been under observation during the past 2 years for dyspeptic symptoms with epigastric and subscapular pains. Two weeks previously she had vomited a little blood. A week later she had a more definite haematemesis, became collapsed, and afterwards passed large tarry motions. As the colon seemed to be overloaded, she was ordered enemata, which at first brought away some rather solid material but later were returned clear. For the last 4 or 5 days she had been complaining of constant pain in the rectum, pain in the lower abdomen, 'bearing down' sensations, and much anxiety and misery. Her doctor was afraid that she might have some malignant disease of the bowel. The patient, who was a multipara, stated that 'the pains were like bad *labour pains*'. *She also had pain on passing water. There was* moderate tenderness over the lower abdomen, more particularly on the left side, where there was a sense of deep resistance suggesting a greatly distended pelvic colon. Rectal examination showed an enormous ball-valve accumulation of faecal material, hard, with a greasy surface, receding before the examining finger, and feeling in shape and size not unlike a foetal head. The examination caused intense pain. On the next day she was given an anaesthetic, the accumulation

was broken up and removed by lavage with prompt relief of all her symptoms.

Matthews Duncan [5] reported a very similar case in which the patient had been thought to be dying of a rectal carcinoma.

CASE 7. A man, aged 63, was sent to me on account of a large hard tumour in the epigastrium. There was also a gland above the left clavicle and a swelling of the right testicle. It was eventually decided that the mass in the epigastrium consisted of retroperitoneal deposits from a malignant growth of the testicle, but in the early stages steps were taken to exclude a primary alimentary carcinoma. For 48 hours or more after the X-ray examination this patient was in the greatest distress, had frequent and urgent calls to stool, and much 'bearing down' pain. Within the space of twenty-four hours he visited the lavatory on thirty occasions, but was never able to pass more than a very small amount of semi-fluid material. He was in hospital and had been treated with purgatives and enemata without result. Neither the resident medical officer nor the sister was familiar with the symptoms. Rectal examination showed a large globular mass in the rectum with a greasy surface; it was extremely hard, and consisted mostly of barium. The examination caused exquisite pain. The mass was finally broken up under an anaesthetic and cleared away with enemata.

It should be noted that with one exception these patients were aged 60 years or upwards. Doubtless their age or infirmity had combined to diminish the expulsive power of the rectal muscles. The clinical symptoms cannot be more concisely described than in the words of Heberden quoted above, but it is necessary to have witnessed the sufferings of these patients to appreciate how severe they may be. Case 6 likened her sensations to 'bad labour pains', and their rhythmical recurrence during the examination was very reminiscent of the pangs of childbirth. In Simpson's cases [3] also the pains were likened to those of labour. Case 7, a very plucky man who bore his illness bravely, suffered great misery and made as many as thirty attempts to empty the bowel in the course of one day. The pain is felt both in the rectum and in the lower abdomen. Presumably as the result of reflex anal spasm the rectal examination in every case caused great pain, resembling that induced by digital examination in cases of anal fissure. The factors

which prevent the evacuation of these faecal masses would seem to include their solid consistency, spherical shape, and smooth greasy surface. In three instances (Cases 2, 6, and 7) the doctor or nurse in attendance had been deceived into thinking that there could be no rectal accumulation because enemata had been returned clear.

Summary

The causes, symptoms, diagnosis, and treatment of ball-valve accumulations of faeces in the rectum may be summarized as follows:

(1) *Causes.* (*a*) A recent gastric or duodenal haemorrhage, a barium meal or enema, or a milk diet. These may impart such a consistency and superficial greasiness to the faecal mass as to render it difficult of passage. (*b*) Dehydration as the result of recent haemorrhage, or of fasting or diabetes. Any of these may help to make the stools unnaturally solid, while the long sojourn of the mass in the rectum results in further desiccation. Robson [6] described 6 cases of 'acute faecal impaction in the rectum' consequent upon diarrhoea or haemorrhage. (*c*) Old age or infirmity. These, combined with the fatigue of repeated calls to stool and reflex anal spasm, diminish the expulsive power of the muscles of defaecation.

(2) The *Symptoms* include: (*a*) Frequent and urgent calls to stool with no result or small fluid results. (*b*) A feeling after evacuation as though there were still something further to expel. (*c*) Severe recurring pain of a peristaltic kind (rectal colic) and lower abdominal colic. (*d*) Painful anal spasms which are intensified by digital examination. (*e*) Difficulty of micturition or actual retention of urine. (*f*) Failure to secure relief by purgatives or enemata unless the mass be first broken up.

(3) The *Diagnosis* is at once made by a digital examination. This reveals a large solid, putty-like globular mass, which often recedes from the examining finger and, owing to its slippery surface, may be difficult to grasp.

(4) *Treatment* consists in the fragmentation and piecemeal removal of the mass, and clearance of the rectum by

repeated lavage. For this operation the administration of an anaesthetic is usually necessary. The handle of a spoon is a useful instrument, although much of the operation must be performed with the fingers. As a preventive measure it should come within the province of the radiologist to advise proper supervision of the evacuations in old or feeble persons who have been subjected to examinations of the alimentary tract after a barium meal or enema.

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XV

VISCERAL NEUROSES[1]

Introductory

In the preface to his book on *Diseases of the Nervous System*, written over sixty years ago, Sir Samuel Wilks remarks: 'It is undoubtedly true that there is not a single organic disease of the nervous system which may not be simulated by a functional and curable one.' The same might be said of diseases affecting the hollow viscera which, depending for their natural behaviour upon a proper co-ordination of vagal and sympathetic impulses, readily complain when this delicate harmony is disturbed or destroyed. That the symptoms of organic visceral disease should be simulated by those of functional disorder is no matter for surprise when we pause to consider that all subjective symptoms express only perturbations of function and that such perturbations may depend upon a great variety of activating or inhibitory stimuli applied at various points in the reflex arc. Angina pectoris, now held to proclaim an ischaemia of the myocardium, is due in most instances to coronary arteriosclerosis, but it may also be caused by coronary spasm resulting from anxiety or tobacco, or occur as a local symptom of anaemia.

Visceral neuroses may be held to include those disorders of visceral motility and sensibility which occur in the absence of organic disease. They are of common occurrence in daily practice, and many of them are trivial in their physical effects, but it must also be conceded that they are capable of causing much bodily distress and anxiety of mind in their victims. Their recognition in most cases is comparatively easy, but in others their differentiation from disorders due to structural disease can be extremely difficult. To regard them as expressive of organic disease is sometimes to do a grave injustice to patients and may even

[1] Based on an address given to the Bristol Branch of the British Medical Association, 30 May 1934 (*Guy's Hosp. Reports*, 1934, lxxxiv. 436).

he ns hurtful in the long run as to label an organic condition 'functional'. Unnecessary invalidism is established and unnecessary operations are performed every day because of these difficulties and failures of differentiation.

I believe that our forebears, before the days of radiological, biochemical, and cardiographic diagnosis, were often more efficient in these differentiations than we are to-day, for although these and other technical refinements have enabled us to understand and to recognize, or to recognize earlier and more surely, a host of structural changes of which we could not previously be sure by the exercise of our clinical wits alone, they have also had the effect of concentrating our thoughts on objective methods and of creating false mechanical and chemical concepts, and, what is worse, of encouraging a certain slackness in clinical history-taking and symptom-analysis. But the pendulum will swing again, and with adjustments of thought and a wiser curriculum it should be possible for the next generation or the generation after that to surpass our own and all others in bed-side wisdom.

It is the purpose of this paper to make a small contribution to the study of the visceral neuroses, by considering the natural history and symptomatology, the differential diagnosis, and treatment of certain neuroses affecting the gullet, the stomach, the colon, the rectum, the bladder, and the heart.

The Nature of the Visceral Neuroses

Of the nature of all of these neuroses it may be said that they are due to a loss of neuro-muscular rhythm. Sir James Paget [1] in a classical paper, 'On Stammering with other organs than those of Speech', in which he discusses the stammering bladder in particular, wrote as follows: 'Stammering, in whatever organs, appears due to a want of concord between certain muscles that must contract for the expulsion of something, and others that must at the same time relax to permit the thing to be expelled.' The result, as with the speech-stammerer, is inhibition or disorderly action with distress or, in the case of some viscera, actual pain.

The victims of visceral stammering are commonly of kindred temperament with the speech-stammerers. Again and again we can trace the symptoms of which they complain to a failure of relaxation of plain muscle, to a positive spasm, or to a loss of the normal tonic and peristaltic habit, disturbances which it has been customary to attribute (employing, I believe, too dubious a term and too narrow a conception) to the influence of 'vagotonia'.

The Mode of Initiation of Visceral Neuroses

(1) The origins of a visceral neurosis may be found in a previous but finally departed organic injury in the shape of an inflammation or irritation. Thus a dysentery may leave in its wake a spastic or irritable colon. A completely cured cystitis may be followed by a nervous frequency. These consequences are closely comparable with the blepharospasm which succeeds a conjunctival irritation, or the asthma which may be initiated by bronchitis.

(2) A visceral neurosis may occur in consequence of a specific sensitization or allergy. Certain dyspepsias and spasmodic disorders of the colon can be traced to food-idiosyncrasies or tobacco, and, although I believe it to be very rare, tobacco-angina may also be mentioned in the same category. As with asthma, however, it is unusual for the symptoms to be traceable always and only to a single specific factor.

(3) External agencies such as cold and the general physical effects of fatigue, emotion, and worry are common precipitating factors or 'triggers' for the visceral neuroses.

(4) The general state of physical tension accompanying chronic anxiety prepares the ground for many of the visceral neuroses.

(5) Commonly enough some combination of the above-mentioned influences can be clearly revealed in individual case histories

(6) In addition to and underlying all these factors, we discover good grounds for including diathesis or the inherited (or constitutional) factor. We know that these visceral disturbances afflict persons of a certain type and temperament, generally recognized as alert, restless, or

'highly strung', and that their occurrence among phlegmatic types is conspicuously rare. We find that multiple visceral neuroses occur simultaneously or at different times in the same individual; that the same visceral neurosis occurs in more than one member of the same family; or that there is a liability to a variety of visceral and other neuroses discoverable in various members of a family. Thus asthma, hay-fever, migraine, and spastic colon will crop up among the near relations of a sufferer from any one of these disorders, and I shall have other associations to describe.

The Mode of Perpetuation of a Visceral Neurosis

Given a super-sensitive nervous mechanism, it is clear that smaller adverse stimuli will be necessary to create or maintain a visceral disturbance than in the case of a more balanced mechanism. In such case a slight degree of constipation, a small dose of purgative, or an indigestible residue in the diet may evoke a tonic over-action in the colon. Again, when cold or fatigue or worry are also operative, the local stimuli requisite for the over-action may be smaller still. This buttressing or reinforcement of one adverse factor by another is, in all probability, a common cause of perpetuation of symptoms.

The anxiety of mind and the physical fatigue and irritability created by the physical symptoms themselves, uncertainty as to their meaning and apprehension of their recurrence, also play their part. Like the conditioned reflexes in Pavlov's dogs, and given an effective initial stimulus, the susceptibility of the patient is constantly increased by repetition. Conversely, in treatment, anything which serves to lengthen the interval between 'attacks' or to eliminate one or more of the conditioning stimuli is calculated to reduce susceptibility.

I believe that our greatest difficulty in the management of cases of asthma, paroxysmal tachycardia, spastic colon, migraine, and all the other paroxysmal neuroses lies, not so much in our inability to discover effective 'triggers' as in our inability to cope with this constantly enhanced

susceptibility or repeated conditioning of the exaggerated reflex by increasingly infinitesimal and varied stimuli.

Oesophageal Neuroses

Among the commoner and less serious oesophageal neuroses we may include 'globus' and 'heartburn', but as these symptoms rarely suggest organic disease I shall not deal with them at length. Both of them will have been an occasional experience for most of us—'globus' in times of grief as the 'lump in the throat', and 'heartburn', sometimes through rush or indiscretion but often enough for no discoverable cause, as an unpleasant burning sensation felt at various levels behind the sternum.

Sometimes, however, these symptoms become so frequent or persistent as to cause much misery, and objective investigations into cause may be completely unavailing. The occurrence of heartburn in the later months of pregnancy suggests that physical or biochemical factors can promote it, but in what way we do not know. Odd circumstances will sometimes cause it. Thus, one man told me that he invariably had heartburn after coitus. Globus is probably due to a local tonic ring-contraction of slight degree; heartburn to increased tonic and peristaltic action [2], perhaps with 'squeezing' of the oesophageal mucosa. As examples of troublesome globus let me quote two cases.

Case 1. The first was that of a nervous Jewish boy aged 14, clever and doing well at school. Up to the age of 12 he had suffered from enuresis. His complaint was that for 18 months he had experienced a feeling of a lump under his sternum, first of all during swallowing and latterly nearly all the time. He also had heartburn. He had seen many doctors and had been X-rayed with negative result. He suffered no difficulty in swallowing or regurgitation and was otherwise very well. Excitement and examinations aggravated the symptom.

Case 2. A married woman, aged 45, had been troubled for a year by a 'lump in the throat', and had consulted orthodox and unorthodox medical opinion and a throat specialist, obtaining no relief. The symptom first developed at a time of great anxiety when she discovered a small breast-tumour. She looked very healthy and had just completed a walking-tour in Germany, walking from 10 to 20 miles a day, and expressed herself as 'bursting with energy'. The symptom,

initiated by a mental stress, had received treatment with medicines instead of reassurance and explanation.

The neuroses of the gullet which simulate organic disease are much more rare. In these spasm giving rise to pain, difficulty in swallowing, and regurgitation of food may occur. They have to be distinguished from benign and malignant stricture, achalasia of the cardia, reflex spasm from benign or malignant ulceration at the cardiac end of the stomach, and the dysphagia with anaemia and glossitis sometimes referred to as 'Plummer-Vincent's syndrome'. Radiology and oesophagoscopy have greatly facilitated these differentiations, but there are usually distinctive features in the clinical history too. The neuroses are characterized by their intermittency and association with nervous causes and with the neurotic temperament. The continued and progressive pain and difficulty, more at first with solids than with fluids, encountered in malignant stricture, and the accurate descriptions of food retention and bulky regurgitation of achalasia are not features of the neuroses, as will be seen from the following cases.

CASE 3. A well-built nervous man aged 49, with a family history of gout in his father and asthma in his son, and a personal history of gout, migraine, and iritis, complained that for 10 years he had been liable at long intervals to attacks of severe pain at the lower end of the sternum, radiating up into the chest and the jaws. He declared that it would be unendurable if it lasted more than a few seconds. This description at once suggested angina pectoris, but further inquiry showed that it had never been induced by walking or effort, that it generally came on while he was stooping over his desk, that it could be immediately relieved if he was able to swallow some fluid or solid, and that on swallowing he heard a distinct click as the pain departed. With reassurance and general treatment the symptoms have remained in abeyance for many months. The patient later consulted me for extra-systoles.

CASE 4.[1] A woman, aged 69, was troubled for a period of 3 years

[1] A recent re-examination of this case has revealed an organic cause for the symptoms. In certain postures only a very small hernia of the stomach through the oesophageal opening can be revealed radiologically. It is worthy of note that this patient showed none of the associated neuroses which are a feature of the majority of the cases described in this paper. Case 3, I now have no doubt, was also a case of hiatus hernia. Globus, heartburn, and painless anxiety dysphagia thus remain the only common neuroses of the gullet.

by a frequent burning sensation in the course of the gullet to which were added curious spasms while eating in which the food would not go down. At times she was compelled to leave the table and bring up a mouthful of food. These episodes were sometimes followed by hiccups. Radiograms showed a normal gullet. A fuller dietary than had been allowed, alkalis, and luminal brought about a marked amelioration of symptoms.

Case 5. A nervous Welsh woman, giving a family history of insomnia, from which she herself suffered, and of 'nervous breakdown' in a sister and shell-shock in a brother, complained of a sensation of 'lump in the throat'. This would be worse at night and on sitting up she maintained that she could hear 'food trickling through it'. On three occasions she had brought up food. She had always experienced difficulty in holding her water. X-ray examination with emulsions of varying consistency failed to reveal any abnormality of the gullet.

Case 6. A nervous woman, aged 43, after a tiring day was seized with an inability to swallow while eating fish. This inability persisted for 10 hours, during which she could not even swallow fluids or her own saliva. There was no pain. During the previous 4 years she had experienced the same symptom on several occasions, but it had only lasted for about 10 minutes. Eating fish when tired had been the chief precipitating factor. There was no radiological evidence of any disease of the oesophagus.

Gastric Neuroses

These are so numerous and varied that they would require a chapter to themselves. They may be expressed by pain, discomfort, nausea or vomiting, flatulence, or anorexia in varying combinations. Air-swallowing is a frequent accompaniment. Those which simulate organic disease such as gastric or duodenal ulcer are the most important in that inappropriate treatments may be deemed necessary and invalidism increased by the idea of graver trouble. Although operations are now less frequently performed for the gastric than for the colonic neuroses there has been too long a tale of them in past years.

In the comparatively few cases of genuine allergic dyspepsia which I have encountered, the symptoms have sometimes been severe enough to suggest organic disease, but histories of food-poisoning or food-idiosyncrasy, an association with urticaria or angio-neurotic oedema, and negative radiological studies have served to complete the diagnosis.

Case 7. A woman of sensitive type and with too little to occupy her, complained of gastric symptoms developing, as in duodenal ulcer, from 2 to 3 hours after food and, also like duodenal ulcer, recurring at intervals of a few months and lasting for 2 or 3 weeks. On inquiry, however, the sensation was not the usual gnawing pain, but a 'feeling of lump in the epigastrium'. This 'feeling of lump' already mentioned as distinctive of globus, may also be described in gastric, colonic, and rectal neuroses. In her case it probably expressed a pyloric contraction occurring when the stomach was empty or emptying. She also mentioned nocturnal attacks of rectal pain, and digital examination showed a rectal ring-spasm.

Case 8. A chronic asthmatic, male, aged 52, complained of 'feelings of constriction' in the stomach, worse when he was empty and eased by food. Radiological examination with the barium meal on two occasions showed only a very rapidly emptying organ and no evidence of gastric or duodenal ulceration.

Case 9. Following upon a gastric upset attributed to fish-poisoning, and accompanied by a generalized rash, a young woman developed dyspeptic attacks characterized by epigastric or hypogastric pain commonly relieved by food. There was marked aggravation by worry, cold, chocolate, and beef. Dietetic care, rest, and belladonna brought partial relief.

Case 10. It is important to remember that the victim of a visceral neurosis may also develop organic disease. As a reminder of this let me quote against myself a further case of an asthmatic and highly nervous Jew who had been troubled for 7 or 8 years by vomiting attacks. Investigated in a well-known clinic in 1924, no organic disease was found. In November 1928 a Berlin radiologist diagnosed ulcer. I saw him in March 1929, for nausea when tired or empty, and found no sign of organic trouble, and again on 5 November 1930, when he brought films from another clinic in Germany purporting to show the scar of a healed duodenal ulcer. Vomiting was now once more a feature, but, persuaded by his general nervous state, I still regarded the case as *one of gastric neurosis with pyloric spasm*. At the end of that month, as he had had sickness again and once vomited raisins at 2 a.m., which he had taken at lunch-time, I had him X-rayed once more. An intense spasm of the pylorus, with some delay, was reported, but no visible lesion. Nearly a year later he was operated on for a carcinoma of the pylorus and did not survive the resection. It is possible that he may originally have had a benign ulcer, but he can scarcely have had a carcinoma for so many years.

Colonic Neuroses

Of the neuroses affecting the alimentary tract the colonic neuroses, after the gastric neuroses, are the most frequent.

They are also more often mis-diagnosed than the others notwithstanding that they present, as a rule, a precise clinical picture and quite commonly confirmatory objective signs. As I have discussed them fully in Lectures XI and XII I shall not dwell upon them in detail. Suffice it to say that the most important type, sometimes called the spastic colon, is characterized by a dull, steady ache or sometimes a much more severe pain in the ascending, descending, or transverse colon and that the colon can often be palpated in its tonic contracted state. It leads to diagnoses of appendicitis (in one-third of a personal series of 50 cases the appendix had been removed), of duodenal ulcer, diverticulitis, carcinoma coli, renal colic, ovarian and tubal disease, and hypochondriasis. Here is a characteristic case:

CASE 11. A medical man, aged 52, consulted me for an abdominal 'ache' of many years standing. The pain was indicated as passing across the middle of the abdomen and down into the left iliac fossa. The bowels moved twice daily, but the stools were commonly hard and fragmentary. In 1927 and 1932 his alimentary tract was X-rayed with negative result. Two surgical friends declined to remove his appendix. At first he used to lose the symptoms on a holiday. He had also been troubled with anal pruritus, from which a brother suffered severely. An elder sister experienced abdominal symptoms like his own. His mother and some maternal cousins had had eczema. Occasionally he had severe rectal spasms, both by day and by night. Further investigation failed to reveal any evidence of organic disease. There were good reasons for considering an allergic factor in view of his family history. Medicinal and dietary measures were signally unsuccessful.

RECTAL NEUROSES

Less frequent than the gastric or colonic neuroses the rectal neuroses are capable of causing greater but fortunately rarer and usually briefer pain than either. In the milder forms there is merely a sensation of 'a lump in the rectum' or of something to be evacuated although the bowel is empty. These might be described as cases of rectal 'globus'. In the severe type the patient is seized with an intense pain in the rectum which may endure from five to twenty minutes or even longer. The pain is described as 'neuralgic' or 'like a bad toothache'; it has a sickening

quality and may be excruciating. It sometimes gives the impression that the coccyx is being forcibly beat inwards. These rectal crises affect both sexes; they are especially apt to occur at night or towards the early hours of the morning. In none of my cases included in this category has there been any evidence of tabes dorsalis. Fainting sometimes results from the pain, which is presumably due to an intense spasm of the powerful local sphincters. Overwork and worry have seemed to me to be precipitating causes. Inflation of the rectum with air may bring relief. So also may firm sustained pressure, inwards and upwards, on the anal sphincter.

Vesical Neuroses

The most familiar neuroses of the bladder are the enuresis of childhood and the inability, so common in nervous men, to micturate in public or in the doctor's presence when a specimen of urine is required. In the first relaxation of sphincters occurs too readily, in the second not readily enough.

Sir James Paget draws a graphic picture of a more exaggerated form of nervous difficulty, in which complete retention may follow upon a nervous and ineffectual straining. In one of his descriptions a man, who had once experienced this disability while out walking with a lady friend, declined ever to go walking with her again because he knew the association of ideas would be too strong for him and would again promote a nervous retention. He also mentions the case of a clergyman who always passed a catheter before going into the pulpit because on one occasion, having experienced an urgent desire to micturate during a sermon, he found himself unable to perform the act when the sermon was over.

Nervous frequency, commoner in women, may be a great nuisance and often follows the physically induced frequency of cystitis.

Nervous incontinence may cause misery as great as nervous retention, and I have notes of one young married woman who suffered the combined miseries of vaginismus, nervous incontinence of urine, and nervous diarrhoea, and had pain both in bowel and in bladder after evacuation. Her

psychology was gravely disturbed and her nightmares were all in connexion with Invntories.

Cardiac Neuroses

I comc lastly to the cardiac neuroses, a most important group on account of the fears which are so readily engendered in the lay mind by the mere suspicion or idea of heart disease. With these cases we have a very special responsibility. Much harm was done in the past by doctors who labclled functional heart disorder as cardiac disease. Equal harm may be done in the individual case by a display of uncertainty as to thc nature or purport of cardiac symptoms. As a whole the profession is now alive to the comparative insignificance of many murmurs, of extra-systoles, and other benign arrhythmias which at one time were doubtfully understood and often too seriously regarded.

Of the cardiac neuroses wbich may cause the most distressing symptoms and so most closely simulate organic disease, I am selecting simple paroxysmal tachycardia and the nervous nnginas. I shall allow a few of my cases to speak for themselves, presenting the bare facts, for brevity, without indicating the considcrable effects produced by these disturbances on mental and bodily health.

Case 12. A man, aged 69, suffered from attacks of paroxysmal tachycardia from his schooldays. These would last from 2 minutes to 5 hours, and always started and ended abruptly. Bromides diminished them and lying down tended to stop them. Latterly he had also developed spasmodic asthma.

Case 13. A man, aged 62, had suffered from bouts of paroxysmal tachycardia lasting up to 8 hours for a period of 18 years. The pulse-rate in the attacks ranged from 160 to 170. He was able to ride and golf and to lead an active life. The attacks would start and end abruptly, and were commonly preceded by a feeling like a tennis-ball below the left ribs (? colonic globus). He himself traced a connexion between the state of his bowel and the cardiac attacks.

Case 14. A woman, aged 72, had been troubled for 20 years by bouts of simple paroxysmal tachycardia, starting and ending abruptly and lasting many hours. Her daughter had similar attacks.

Case 15. A medical student, aged 21, suffered from attacks of paroxysmal tachycardia with pulse-rate varying from 180 to 200 to

the minute. The attacks started and ended abruptly and were commonly arrested by lying down. He also had asthma and was a very bad stammerer. He continued to play 'rugger' without ill effect.

In these four cases we have exemplified the familial occurrence of paroxysmal tachycardia; associated paroxysmal neuroses—tachycardia and asthma—in the same individual; and finally, in Case 15, 'stammering' in no less than three departments—speech, heart, and bronchial tree. In each case long continuation of the cardiac attacks without physical deterioration or mishap was manifest. The majority of patients with a visceral neurosis are afflicted with nosophobia in greater or less degree. Reassurance alone will never cure paroxysmal tachycardia, but it can remove unnecessary dread and contribute to general well-being and sometimes a normal way of life, and is therefore an essential element in the treatment of cases. Care may be necessary to distinguish simple paroxysmal tachycardia from such conditions as auricular flutter and paroxysmal fibrillation.

Let us pass finally to a consideration of certain distressing attacks which simulate, in one particular or another, the dreaded 'breast-pang' or angina pectoris. There are cases in which only careful watching over long periods, with or without electro-cardiographic studies, can make the distinction between the graver and the more benign disease. The label of 'pseudo-angina' has been used in the past to describe the nervous and more innocent condition, but since sternal pain with arm-reference and angor animi may characterize both types, and the pathology of symptoms, if not of cause, is surely identical, and since in both the symptoms are real enough, the nomenclature is surely undesirable. A nervous dyspepsia which simulates peptic ulcer is not a 'pseudo-dyspepsia'. It were better to speak of nervous or vasomotor angina than of false angina. A number of these cases of nervous origin fall into the category of the vasovagal attack, as defined by Gowers, and as such I prefer to classify them both for purposes of clinical study and therapeutic reassurance. In such cases there is commonly a sense of substernal or praecordial discomfort or oppression and sometimes of very real pain. Reference to

the neck and left arm also occurs. The feeling of impending death, which probably obtains in less than 20 per cent. of cases of angina of effort due to coronary disease, is present in the majority of the vasovagal cases and often overshadows the physical distress. The relationship to effort is much less precise than in the organic cases, the duration of the attacks is longer, the age-incidence is younger, and female cases are more numerous. A low state of physical health coupled with anxiety of mind are the most evident predisposing causes.

Pallor, coldness, and fluctuating blood-pressure, and a quick or very slow pulse are the objective features of the attack.

Case 16. A small, highly strung woman, aged 37, and a 'martyr to migraine' lost her husband suddenly. She suffered great grief and was referred to me with a complaint of attacks of praecordial pain and a sense of constriction over the sternum, coming at rest or with effort and often waking her at 1 a.m. and lasting for as long as 1 hour. It had become impossible for her to push her child aged 3 in the pram. Later I saw her for different attacks in which she 'felt dreadful' and 'not at all as with an ordinary faint'. With these she became very cold and experienced tightness in the chest and her 'heart felt enormous'. She had a low blood-pressure and there was no evidence of cardiovascular disease.

Case 17. A man, aged 36, who had suffered from anxieties and prolonged insomnia, having had some 'nasty sensations' through the day, was seized with palpitations and praecordial pain shortly after getting into bed. He also experienced a sense of impending death. His heart seemed to beat forcibly rather than fast. There was no sign of cardiac disease and his blood-pressure was low, and his pulse-rate 56. I reassured vigorously, prescribed bromides with arsenic, wine with his dinner, and a good holiday. His doctor wrote 5 years later to say that he had remained perfectly well ever since.

Summary and Treatment

We find, then, that the visceral neuroses affect persons and families endowed, usually, with the neurotic temperament in greater or less degree; that there is, as many of my case-notes show, a frequent association of two or more neuroses in the same subject or the same family; that specificity of cause is usually lacking, if we except some rare instances of idiosyncrasy or allergy; but that influences such as

fatigue, worry, and cold may all be contributory. The disorders are in no sense hysterical. The symptoms may be sufficiently pronounced to suggest organic disease, but intermittency, periodicity, the mode of occurrence of the attacks, the precipitating causes, and negative physical studies should generally serve to complete the differentiation. The treatment is the treatment of the individual patient. Explanation, reassurance, and the accepted sedatives and anti-spasmodics including bromides, luminal, and belladonna, all play their part. At times it may be necessary to take a strong stand against surgery and other physical treatments such as rest in bed or elaborate dietetics which may have been injudiciously prescribed. Every endeavour should be made to improve the physiological and psychological balance by a sensible adjustment of conduct and affairs. By such means, and not by concentrating our attentions on the stammering organ, are we most likely to do service to patients whose sufferings are always inconvenient and sometimes as real and disabling as those caused by structural disease.

It is exactly fifty years since the late Sir Clifford Allbutt [3] published a brief monograph, based on his Goulstonian Lectures relating to the visceral neuroses. The lessons which he taught have never been so widely assimilated as they should have been, and his little book is all too little known. We have advantages in the shape of diagnostic method and appliances which he did not possess and much new physiological and psychological knowledge to help us in our studies. If we, in our generation, can learn to leaven our newer methods with some of his clinical wisdom and humane philosophy, the next fifty years should add much to our understanding of these interesting and prevalent disorders.

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XVI

THE NATURAL HISTORY, PROGNOSIS, AND TREATMENT OF STAPHYLOCOCCAL FEVER[1]

It was customary for the older physicians, untroubled by a plethora of laboratory and specialist information, to study in their broad outlines, but with full attention to clinical detail, the natural history of the diseases which confronted them in practice. For this reason their descriptions, although less complete, are often more vivid and more illuminating than those of the present day. Gull, in our own school, decrying 'a narrow pathology', was insistent on the value of what he concisely called 'the general view', and his wide comprehension, sure balance, and power of instruction are evident in all his writings. To-day the 'general view' is rarely taken, the journals are filled with separate comments on disease from the pen of the bacteriologist, the biochemist, and the medical or surgical specialist, and under the influence of their opinions, often too limited and lacking co-ordination, medical philosophy and the arts of prognosis and treatment have not uniformly prospered. There must of necessity be few now in the profession who are so widely instructed and so constituted that they can take a wholly unbiased view of a disease; who can read at once the effect upon its type and course of heredity, environment, and personality; who can gauge the proportionate chances of infection and immunity; who can visualize behind the clinical image the intimate processes of organ- and tissue-function; who can assess the relative importance of modern objective methods and subjective symptoms; who, applying simultaneously the lessons of anatomy and morbid anatomy, of physiology and morbid physiology, can think both surgically and medically. The subject has grown too vast. Nevertheless, for the preservation of balance it is essential that the 'general view' be taken from time to time, and that better attempts at co-ordination of experience be made.

[1] This and the two ensuing papers were introductory to Symposia in the *Guy's Hospital Reports* (1930, 1931, and 1932) dealing with some common infective processes.

For this purpose the symposium, whether of the journal or the medical society, is a convenient method.

In selecting for review the local and general consequences of staphylococcal invasions we are selecting a type of disease well suited for consideration by this method. Staphylococcal infections are at all times prevalent. They are a part of the daily material of the general practitioner and the out-patient department. They produce complications which fall within the province of the general physician and the general surgeon. They provide problems for the dermatologist, the bacteriologist, and other specialists. They create important difficulties in differential diagnosis. There is much uncertainty as to the value of the immuno-therapeutic and chemo-therapeutic measures often employed to combat them. While infection most frequently remains confined to the skin in the shape of boils or a carbuncle it may lead to a bacteriaemia or a septicaemia, and to a group of sequelae so varied that staphylococcal fever may well be regarded as one of the most protean of infective diseases. It is usual for these sequelae to be separately considered. How much less satisfactory would our understanding of typhoid fever and pneumonia be if we were thus to subdivide them into a number of separate diseases in accordance with their local and special types of complication. How much more satisfactory our understanding of general staphylococcal infection becomes when we regard it, in common with typhoid and pneumonia, as a specific fever it is one of the purposes of this paper to show. For the rest, the remarks which follow are intended as an introduction to contributions by my colleagues in exposition of surgical and other aspects of the disease.

Under the title of staphylococcal fever I shall include all the immediate febrile consequences, together with their *metastatic* accompaniments, which may from time to time complicate a boil or carbuncle.

With illustrations from a small series of cases personally observed I shall endeavour to depict the natural history of staphylococcal fever, to consider in brief the difficulties in *diagnosis* and *differential diagnosis* which it may present,

and to discuss prognosis and the merits of the therapeutic methods now in vogue.

Of the general pathology of diffuse infections with *Staphylococcus aureus* we may say firstly that they have, in nearly all cases, a primary skin focus. Mucosal invasions may occur, but this is less certainly established. The focus may be in the guise of a pimple, a stye, a solitary boil, a widespread furunculosis, a carbuncle, or an infected wound or abrasion. From time to time, and more commonly than is generally appreciated (although fortunately still in a minority of cases), fever follows of short or long duration. In a considerable proportion of all cases of staphylococcal fever there is a true bacteriaemia or septicaemia with, or only very occasionally without, multiple metastases or a solitary metastasis.

Staphylococcal fever is a disease more particularly of childhood and young adult life, but there are strikingly different liabilities in the different age-periods. In children metastasis in bone, leading to acute osteomyelitis, is the usual sequel. A long bone is the site of election, or more rarely some part of the pelvic girdle. With prompt and adequate treatment the disease may here become arrested. In unfavourable cases there is a continuance of the original septicaemia or a secondary septicaemia develops with dissemination of multiple small abscesses into the kidneys, the heart, and the lungs. In adults osteomyelitis is rare and a boil or carbuncle of the kidney with resulting perinephritis or perinephric abscess is the more usual sequel. Some authors have referred to staphylococcal perinephritis as though it could occur by direct metastasis into the peri-renal cellular tissues. My experience suggests that it is invariably secondary to a sub-capsular renal boil or carbuncle (see Ryle, J. A., *Brit. Journ. of Urology*, 1938, x. 337). Without serious pyaemic manifestations metastases also occur in the prostate, or in muscle. In the graver cases with septicaemia multiple lung abscesses are common. Abscesses in the skin are not infrequent. A solitary focus in the tibia may become imprisoned and lead to a chronic Brodie's abscess. Rarer sites for a secondary abscess are the brain

or a vertebra. Both in children and in adults it is clear from clinical histories and a knowledge of environment and antecedents that staphylococcal fever, whether benign or malign, is infrequent under good general conditions of life and health. Osteomyelitis is more a disease of the city hospital than of private practice among the comfortably situated; perinephric abscess or septicaemia in an adult is commonly the end-result of lowered vitality through recent illness or overwork. The well-known occurrence in some persons of furunculosis relapsing over long periods has suggested that natural immunity may be so far lost that an actually increased sensitiveness to the staphylococcus becomes established, such a sensitiveness being regarded by some as akin to the specific types of sensitiveness shown in the allergic disorders. Even a serious staphylococcal illness successfully weathered does not necessarily confer lasting immunity (*vide* Cases 1, 7, and 9). A small focus may also lie latent for months or years and then give rise to a fresh generalized or metastatic infection (Case 9?). I have also seen, on more than one occasion, a staphylococcal infection pave the way for a streptococcal septicaemia.

In diabetes it has long been recognized that there is an increased liability to boils and carbuncles. On the basis of this knowledge it has been supposed that, without diabetes, an excessive consumption of sugar and starch may predispose to staphylococcal infection.

The terms bacteriaemia and septicaemia (or pyaemia) are employed with special reason. In each case it is to be inferred, from the fact that distant metastatic infection occurs, that organisms have found their way into and been disseminated by the blood-stream. In bacteriaemia the stage of transit has been comparatively uneventful and unaccompanied by such evidences of grave activity as repeated rigors or high swinging pyrexia. The cases are commonly seen first or diagnosed first in the stage when local symptoms of an abscess have developed and the opportunity of proving a stage of bacteriaemia by blood culture has passed; the fever terminates when the abscess is drained. In septicaemia or pyaemia an initial rigor or recurrent rigors, pro-

fusc sweats, high sustained or swinging pyrexia, sometimes continuing for many weeks, and multiple abscesses announce only too plainly to the clinician what blood culture may readily confirm, namely, the presence of thriving organisms in the circulating blood. This distinction between a bacteriaemia and a septicaemia may seem arbitrary, but it is clinically important. It is perhaps a question of degree of infection, or it may depend in some instances on the readiness with which certain tissues show themselves capable of forming a spontaneous fixation abscess. We can at present do no more than guess at the relative determining influence of the numerical factor on the part of the invaders and the particular qualities of the defence. We know that some constitutional types support infection less well than others.

The cases (1–9) described hereunder have been taken from my private case-notes in chronological order and without selection. Case 10, which was referred to me at my Out-Patients and was later admitted to Clinical Ward under the care of Dr. E. P. Poulton, is included as an example of ambulant staphylococcal fever with metastatic abscesses in muscle, tonsil, and skin.

Case 1. *Furunculosis. Staphylococcal fever (bacteriaemia). Perinephric abscess. Recovery.* I was consulted on 20 September 1921 by a newly qualified medical man, aged 25, then holding a house-appointment. For several weeks he had been feeling unfit, but had been playing football for the hospital. He had a slight cough. A few mornings previously he had wakened with blood in his mouth and on the pillow. His temperature was 100. There were no physical signs of lung disease and no tubercle bacilli were found in the sputum. He had recently had boils and a slight antral infection. He got well and again played football. On 1 December 1921 I was asked to see him in his own home, where he had been lying for a fortnight under suspicion of paratyphoid fever. His illness had started with a chill. He had then run a remittent pyrexia with temperatures ranging between 101 and 104. There had been an occasional sweat and a slight cough. Bowels normal. Tongue fairly clean. No splenic tumour. No rose-spots. No T.B. in sputum. Negative agglutinations against organisms of the typhoid group. For 4 days past he had had pain in the left lower chest and left loin on coughing or deep breathing or turning over in bed. There was tenderness and contraction of the rectus on palpating under the left rib margin. Air-entry was deficient at the left base, but there was no pleuritic friction. There was a very

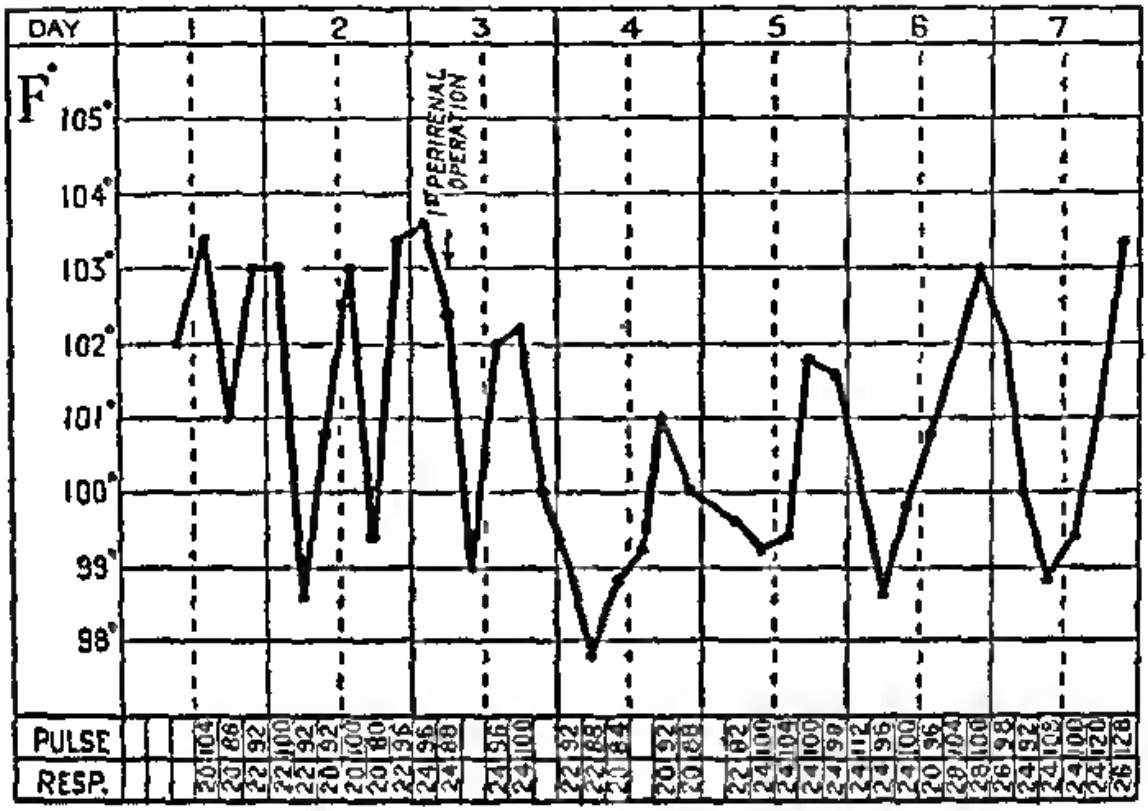
tender spot over the last rib and in the last space on the left and very slight tumefaction of the loin. Leucocyte count 20,000 cells per c.mm. Urine normal. A provisional diagnosis of perinephric abscess was made and he was sent into hospital. In the ward his temperature came down in step-ladder fashion, his leucocytes fell to 15,000 per c.mm., but loin tenderness and impaired movement of the left diaphragm persisted. On 6 December 1921 the temperature was normal, but there was definite swelling in the loin. The signs of lung compression reached the angle of the left scapula, but no fluid was obtained on needling. Mr. R. P. Rowlands opened a walled perinephric abscess of the size of a golf-ball in the left post-renal space. The massive collapse of the left lower lobe persisted for some time. Otherwise recovery was uneventful. I saw him again on 18 March 1922 for boils on the neck and chest following a follicular tonsillitis. Since then he has kept well in a busy practice.

Case 2. *Furunele. Staphylococcal fever (septicaemia). Renal, cerebral, and lung abscesses. Death.* A man, aged 35, of rather fat unhealthy type, was taken ill with a cold then prevalent in his house on 25 October 1923. He had remained feverish up to the day of my visit on 3 November 1923, when his temperature reached 104. On 29 October 1923 he had drawn the attention of his doctor, the late Dr. E. Hardenberg, to a boil on the left wrist which had already been there some days. He complained of pain low in the left chest aggravated by deep breathing or rolling on to his right side. His tongue was furred. He looked ill and limp. There was an area of exquisite tenderness no larger than a florin immediately below the 12th rib on the left side. Urine normal. Leucocyte count 14,000 per c.mm. A Widal test had already been performed with negative result. On 5 November he developed right-sided pleuritic pain and began to cough up sputum, at first rusty, then sanguineo-purulent. On 10 November temperature swinging; pulse 98–100; respirations 36–40. Left flank signs subsiding. Impaired note at right base with distant tubular breathing. Leucocytes 13,000 per c.mm. On 16 November after a definite improvement with a drop in the temperature and diminishing signs at the right lung-base, he developed a left femoral thrombosis. In spite of this his general condition appeared good and his mental outlook was more cheerful. A week later he had abdominal distension, became unconscious, and developed a squint and slight head retraction; his temperature rose to 103 and he died, presumably from a cerebral abscess.

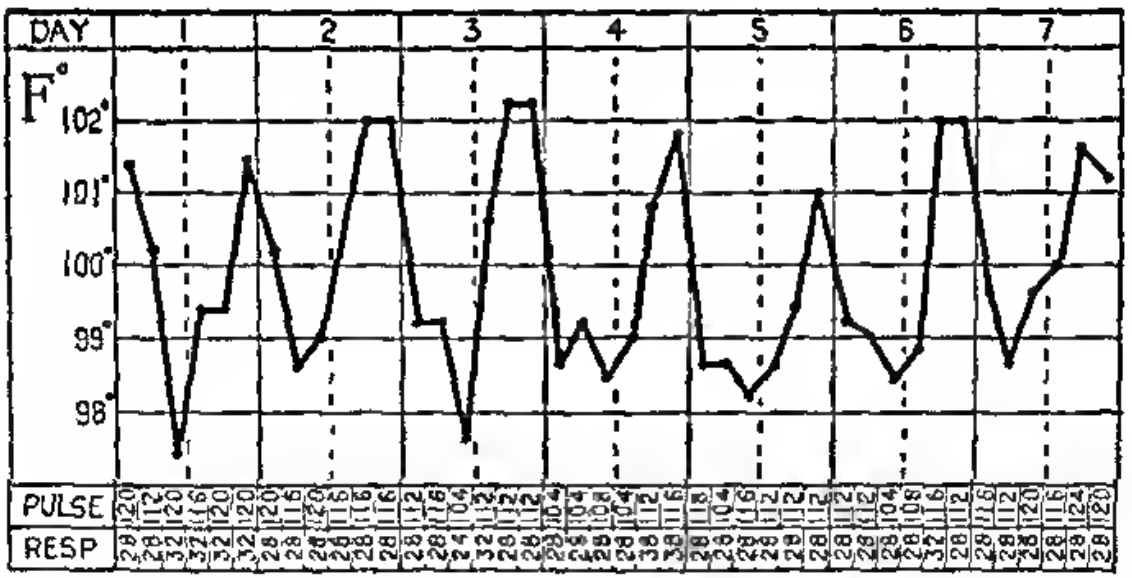
It is noteworthy that this man was of unhealthy type and that he never showed a good leucocytic response. Nevertheless, I have since wondered whether early operation on the left kidney or drainage of the perinephric tissues might have saved his life.

CASE 3. *Furuncle. Staphylococcal fever (septicaemia). Abscesses in kidney, lung, skin. Recovery.* **This was the case of a medical man**

CASE 3 (1ST WEEK)



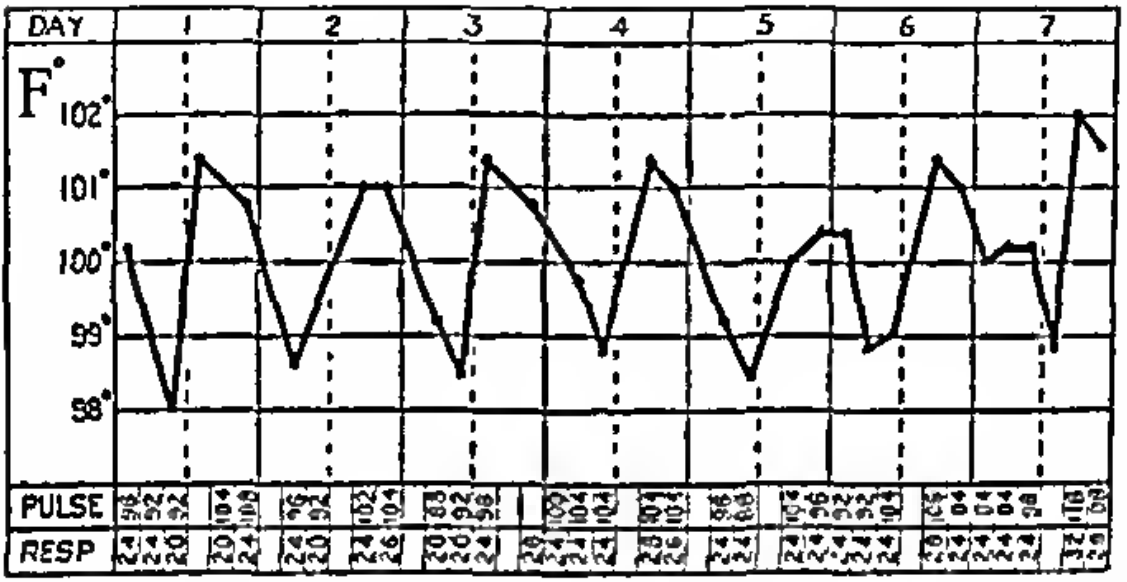
CASE 3 (5TH WEEK)



aged 32 (*seen 2 July 1927 in consultation with Dr. Richard Clarke of* Bristol), who 6 weeks previously and 10 days after the healing of an obstinate boil on the chin, developed high pyrexia with left loin discomfort. Staphylococcal septicaemia was soon afterwards diagnosed

and confirmed by blood culture. Within a fortnight of the onset the left loin was incised an account af tenderness, but the kidney was not apparently explored and no pus was found. There was a leucocytosis varying fnom 18 ta 20 thousand cells per c.mm. On 22 June the loin wound had been reopened on the advice of Dr. A. F. Hurst and some pus found. A week later he became desperately ill with signs of effusion in the left chest. Blood-stained fluid was obtained with the needle and the effusion was drained with n catheter detween the ribs. On a few occasions he had coughed up muco-pus.

CASE 3 (0TH WEEK)



When I saw him he had developed several small deep abscesses on the trunk, aver both breasts aad the back. He looked very ill, was hectic and wasted and tremulous like a third-week typhoid case. After my visit he coughed up blood and pus on several occasions and had patchy signs in both lungs. During this anxious phase there were rigors. Nevertheless he weathered the storm. His temperature became normal on 15 August, 12 weeks after the onset of his illness, and his restoration to health was complete. The specimen charts are taken from the first, fifth, and ninth weeks of observation. In the earlier stages he was given injections of racrcurochrome, which gave him a slight enteritis and in his opinion brought no benefit.

CASE 4. *Staphylococcal fever (septicaemia). Lung abscesses. Osteomyelitis of femur. Recovery.* On 30 October 1925 I saw, in consultation with Dr. W. O'Brien of Brockley, a well-built, intelligent boy, aged 16, who had been taken ill 4 days previously with upper abdominal pain aggravated by breathing. He had a high fever, looked gravely ill, was breathing fast, and there were signs of right basal pleurisy. On the previous night he had also developed great pain in the lower portion of the right femur. The thigh was swollen here and exquisitely tender. The knee-joint was not involved. He was ad-

mitted to Guy's under the care of Mr. F. J. Steward. An operation was performed for osteomyelitis of the femur. Blood cultures grew *Staphylococcus aureus*. For many weeks this boy was desperately ill. He developed many lung abscesses, especially in the left upper lobe, with considerable bright haemoptyses. Fluid aspirated from the left pleural sac grew *Staphylococcus aureus*. At one time and another in the early stages he was given mercurochrome and vaccines without the slightest evidence of any good effect on his symptoms or pyrexial curve. He eventually made a good recovery, but was re-admitted later for sequestrectomy.

Case 5. *Furunculosis. Staphylococcal fever (septicaemia). Recovery.* On 3 February 1929 I saw, in consultation with Dr. A. E. Gow and Dr. James Rannie, a dental surgeon, aged 34. For 2 or 3 years this patient had been unfit, originally with a carbuncle and since then with recurrent furunculosis. During the past month he had had a troublesome boil on the right thigh. A fortnight previously he had had influenza with laryngitis. A few days later he developed a cough with patchy pneumonic signs at the right base. His temperature had remained high (102–5), pulse-rate rarely above 90, respirations 20. There had been some purulent sputum, occasionally tinged with blood, from which *Staphylococcus aureus* was grown. There had been one rigor at the beginning of the illness and one in the past 24 hours. He had been treated initially with a pneumococcus immunogen. Subsequently he had had two doses of a vaccine and an intravenous injection of mercurochrome. None of these measures had in any way influenced his symptoms or his temperature curve. He was a dark, stocky type of man and well covered. He 'looked septic' and was clearly very ill. There was a recent stye on the right lower eyelid. The spleen was not palpably enlarged. The chest was clear except for rhonchus at the angle of the right scapula. Staphylococcal septicaemia was diagnosed, and this was confirmed by blood-culture. Symptomatic treatment with a copious fluid intake was advised. I next saw him on 15 February. High pyrexia had continued and there was a duller note at the right base. That morning he had been seized with sudden severe pain in the right upper chest in front together with great difficulty in breathing. The liver dullness was seemingly diminished and I queried a small anterior pneumothorax. There was a wide band of cutaneous hyperalgesia corresponding with three or four of the upper dorsal roots. I did not see the patient again, but I learned that the illness continued uneventfully until he developed an acute streptococcal tonsillitis a week or two later, for which he was given antistreptococcic serum. He then made a complete recovery.

Case 6. *Staphylococcal fever (septicaemia). Pulmonary abscesses. Blood-stained pleuritic effusion. Recovery.* A man, aged 28 (seen in consultation with Dr. A. J. Williamson of Watford, 13 April 1929), gave a history of an 'ordinary chill' 3 or 4 weeks previously. He

remained at work for several days, but then became more seriously ill. On 3 April he was admitted to hospital with high fever, sustained at first, but swinging latterly. With this he had profuse night-sweats, and cough with nummular, purulent sputum just beginning to be streaked with blood. Pleuritic signs had appeared at the right base on 11 April, but only a small quantity of clear fluid was obtained on needling. A provisional diagnosis of acute pneumonic pulmonary tubercle had been made, but no bacilli were reported in the sputum. The patient looked to me not phthisical, but septicaemic. He was muscular, well-covered, bright-eyed, and still alert and vigorous. The tongue was fairly moist. There was one large yellow follicle on the right tonsil. He gave no history of boils or cutaneous sepsis. There was no loin tenderness. There were signs of a large effusion in the right chest which I needled, withdrawing intimately blood-stained serous fluid. Later needlings of the chest gave similar slightly turbid blood-stained fluid. Cultivations both from the fluid and from the blood grew *Staphylococcus aureus*. The patient made a complete recovery, interrupted only by a small saphenous thrombosis.

CASE 7. *Furunculosis. Staphylococcal fever (bacteriaemia). Perinephritis. Recovery.* A medical man, aged 42, who had had a staphylococcal infection with prostatic abscess during his war-service, had some small boils in June 1929. At the end of that month he had a solitary rigor and thereafter was laid up with a swinging temperature for 2 weeks. The temperature then subsided, and he got about again but remained unwell, with symptoms and signs of irritation of the left psoas muscle. He had slight scoliosis and was compelled to walk in a constrained, slightly stooping attitude, and could not easily bring the heel of the left foot to the ground. His tongue was brown and he looked 'poisoned'. There was tenderness and 'guarding' in the left loin. At an earlier stage he had had pain and tenderness in the left iliac fossa, and he remarked that 'he was sure he would have had his appendix removed if the pain had been on the right'. There was slight impairment of respiratory movement and percussion note at the left base. Mr. E. C. Hughes, with whom I saw him in consultation, operated on 1 August 1929, incising the loin, where he found hard, oedematous, peri-renal fat, but no actual pus. A drainage tube was inserted and through this a very small amount of sero-sanguineous fluid was later discharged. A complete recovery followed.

CASE 8. *Furunculosis. Staphylococcal fever (bacteriaemia). Perinephric abscess. Recovery.* The patient, seen 10 January 1930 in consultation with Dr. C. H. Hall and Mr. A. S. Gough of Watford, was a robust young man and a keen footballer. Between 20 December 1929 and 23 December he was apparently suffering from slight chills, as 'he kept asking to have the windows shut'. He then developed pain in the left loin passing down the left leg, and was found to have some pyrexia. After a trousient improvement he became worse and was

sent into a nursing-home, where he continued to complain of pain in the left loin and had frequent night-sweats. His temperature had been swinging between the base-line and 102 or 103. His pulse-rate, normally 60, had not exceeded 70 to the minute. Turning over in bed, a sudden deep breath, and stretching out the left leg all aggravated the pain. There was guarding of the left loin muscles, slight *tumefaction*, and a *single spot of exquisite tenderness below the last* rib. There was impairment of movement and entry at the left base. There was a well-marked *leucocytosis* (20,000 cells per *c.mm.*). A perinephric abscess was diagnosed and drained by Mr. Gough the next day. A satisfactory recovery followed.

Case 0. *Staphylococcal fever (septicaemia) with lung abscesses and right perinephric abscess. Recovery. Four years later recurrence of infection in the left kidney with perinephric abscess.* A young medical man was troubled in 1923 by symptoms relating to the left hip. Varying opinions, medical and surgical, were given, and tuberculosis of the joint was discussed. No final diagnosis was made and the symptoms eventually departed. Between that year and 1026 he had a bad carbuncle on the neck. In 1926 he was in hospital *for several months for* a very serious illness with haemoptyses, pulmonary signs, and sweats. For a time he was thought to have pulmonary tuberculosis. Eventually a large perinephric abscess on the right side was found and drained. He made a complete recovery and returned to practice. Early in February 1930 he developed pain in the left loin, of no great severity at first, and with it pyrexia. A fortnight later a left perinephric abscess localized and was operated on by Mr. F. J. Steward. *Staphylococcus aureus* was grown from the pus. The pyrexia, however, did not subside and he continued to run a high swinging temperature with night-sweats. His urine was found to contain red cells, pus cells, and a *few granular casts; staphylococci were also grown.* There was slight pain at the end of micturition. In spite of the high temperature, which varied between 102 and 104, the pulse remained proportionately slow, the tongue was clean, and food and fluids were partaken of freely. For a time there were signs of diaphragmatic inhibition with lung compression at the left base, but these had disappeared when I saw him for the first time in consultation with Dr. A. H. Douthwaite and Dr. D. Whitlock on 25 March 1930. There were no signs of local infection elsewhere than in the left loin. Prostate gland slightly *tender but not enlarged. There were no clinical signs pointing to a* general septicaemia and blood cultivations had been repeatedly negative. The urinary findings and symptoms taken in conjunction with the fever clearly suggested that the whole of the renal sepsis had not been 'tapped' in the course of draining the perinephric abscess. Mercurochrome had been given without apparent benefit. After a long illness recovery was complete.

This is the only case in my experience in which such urinary find-

ings were present. As a rule the urine in perinephritis is free from blood, pus, albumen, and casts. From this it might be argued that the kidney is not primarily involved, but it may equally be advanced as evidence that the renal abscesses are generally small and localized in the cortical zone, and that they tend to erupt spontaneously on the surface of the kidney. There was no history of any recent cutaneous lesion. Scanning the history of this case it is interesting to speculate (1) whether there had been a focus lying dormant ever since the septicaemic illness in 1920, and (2) whether the suspected left hip-joint disease in 1923 may have been due to an undiscovered staphylococcal infection of bone or soft tissues in that neighbourhood.

Case 10. *Infected abrasions. Staphylococcal fever (bacteriaemia). Abscesses in skin, muscle, and a tonsil.* A boy, aged 13, was referred to my Out-Patients by Dr. H. E. Battle on 28 February 1929 for small tumours of the back, right forearm, left thigh, and left buttock. The first three were superficial and not tender and were situated in the dermis. The fourth was deep in the muscle and tender. Cultures from all of them grew *Staphylococcus aureus*. A culture from a tonsillar focus grew *Staphylococcus aureus* and a streptococcus. Blood cultures remained sterile. The boy complained of no general feelings of illness, but was found to be running a temperature with morning intermissions and evening rise. The spleen was palpable. Leucocyte count 16,000 per c.mm. For 3 weeks he had been suffering from septic abrasions over both heels. The large abscess in the buttock was drained. The temperature did not settle completely for a month.

Discussion

From these cases of staphylococcal fever some instructive conclusions in respect of aetiology, differential diagnosis, prognosis, and treatment may be drawn.

Aetiology. In this small series all ten cases were males; I have a strong impression from cases seen elsewhere and subsequently that the incidence of staphylococcal fever is higher in the male sex. Their ages were between thirteen and forty-two years. The influence of preceding ill health is suggested by the histories of Cases 1, 2, and 5. Cases 3, 7, and 9 were in overworked medical men. Case 10 was that of a boy in poor circumstances and not well cared for. In seven of the ten cases there was a clear account of a primary focus in the shape of a boil or other cutaneous sepsis.

Differential diagnosis. A diagnosis of typhoid group infection had been seriously considered during the initial fever in Cases 1 and 2. The possibility of pulmonary tuberculosis

was discussed in Cases 1 and 6. In Case 9 pulmonary tuberculosis was the initial diagnosis in a previous attack of severe septicaemic staphylococcal fever. Case 5 was for a short time treated as an influenzal pneumonia. Case 7, a medical man, had a scoliosis and a painful and difficult gait which, with an inadequate history, might have led to a diagnosis of spinal or hip disease. A girl recently under the care of Dr. Hurst and myself in Clinical Ward with perinephric abscess had attended an Orthopaedic Out-Patient Department as a spinal case for many months. Case 7 also confessed that his abdominal pain in an earlier stage, had it been on the right side, would almost certainly have led to an appendicectomy.

The differentiation from typhoid fever depends upon the discovery of a present or recent primary focus of infection, the absence of conspicuous splenic enlargement, rose-spots, and intestinal symptoms, and the presence from the beginning of a leucocytosis. The pulse in staphylococcal fever is frequently slow in proportion to the temperature, a small point which may lend support to a suspicion of typhoid infection. Haemoptyses and night-sweats and pleuritic effusion may very well suggest a diagnosis of acute pulmonary tuberculosis, but again the leucocyte count, the history, and sputum examinations should help to decide the issue. I should like to emphasize the frequency and diagnostic significance of sweats in staphylococcal fever, whether due to a focal or general infection. After tuberculosis and infective endocarditis it should be regarded as one of the most important of the 'sweating' fevers. The diagnosis from streptococcal fever can commonly be made on the history and particularly on the nature and site of the initial lesion. In streptococcal septicaemia rigor is more common and sweating less common; glossitis, diarrhoea, rapidly developing anaemia, and splenic enlargement mark the infections with a haemolytic streptococcus, and are absent in staphylococcal fever. The streptococcus selects the joints, the pleura, and the pericardium for its metastatic infections and does not produce the multiple small abscesses in the soft tissues and organs named above as favoured by the staphy-

lococcus. A rapid pulse from the beginning is more frequent in streptococcal than in staphylococcal fever.

Prognosis. With every case of septic fever there is a necessary sense of alarm, but too often alarm verges upon panic or despair. It is true that certain septicaemias, and notably those fulminant streptococcic infections to which the surgeon, the pathologist, and the puerperal woman fall victim, may pass almost immediately beyond human control in the absence and sometimes in spite of prompt chemotherapy or penicillin treatment, but, if these be excepted, and they are the minority, I have never yet seen reason to regard the septic fevers more anxiously than, for instance, the typhoid group of fevers. A reasonably optimistic prognosis, which recognizes the natural tendency of otherwise healthy patients to recover from their acute bacterial illnesses, has a real practical value and may considerably influence the handling of cases. Prognosis depends more for its accuracy on a knowledge of the natural history of a disease than on any other circumstance. The present small series only supports my experience of other cases of staphylococcal fever seen during the war of 1914–18 and in hospital. Given a sound physique, a reasonably early diagnosis, a good leucocytosis, and watchful care, the majority of cases should recover, although the course of the disease is often very prolonged. In this series, after excluding those of lesser severity and labelled as bacteriaemia—cases which determined their favourable course and recovery by forming a spontaneous fixation abscess—we are left with five gravely septicaemic cases, and one case of serious renal infection. Of the five septicaemic cases one died. The remainder made complete recoveries with the exception of Case 4, in which local disability from the damaged femur is likely to persist. In the fatal case the adverse features from the beginning were an unhealthy type of physique, notoriously non-resistent to infection, and a poor leucocytic response. In addition, surgical treatment of the primary focus was delayed and an important secondary renal focus was not touched. Finally, the accident of a cerebral metastasis determined death at a time when there had been definite clinical improvements in respect of general

physical and mental symptoms. It might be argued that the remaining four cases were not representatively severe. As a matter of fact and in terms of hospital classification, all would have found a place on the 'danger list' over periods of many weeks. Multiple cardiac and cerebral metastases are probably always fatal, but pulmonary abscesses, even in great numbers, are consistent with perfect recovery, and without surgical interference as they are spontaneously evacuated.

Treatment. If an appreciation of the natural history of a disease is important for prognosis it is equally or more so for treatment. A further reference to the methods and opinions of Sir William Gull may here be deemed appropriate. At a time when various remedies for rheumatic fever were being vaunted, Gull decided that without a knowledge of the natural course of the untreated disease it was impossible to judge the efficacy of therapeutic measures. He therefore reported with close care and the collaboration of Dr. H. G. Sutton a series of cases treated, apart from nursing and symptomatic measures, by mint water alone.[1] His conclusions were to the effect that there was no evidence that the course of the disease was influenced by the supposedly specific remedies. The work was a model of reasoned clinical research. It is to be wished that judicial inquiries of this kind were more prevalent to-day. For over twenty years in septic states sera, vaccines and non-specific chemotherapy were in fashion, but it must be confessed that their prescription commonly had as slender a basis in reason and systematic controls as had the old rheumatic remedies. Their advocacy could be traced largely to the laboratory specialists, whose training and primary interest were in respect of the agents of disease, whose contacts with patients were small, and who had in consequence but a nodding acquaintance with the natural history of disease. Whatever virtue vaccines may have in the case of local infection I have never been able to understand their rationale in a generalized infection. When

[1] '*Cases of Rheumatic Fever, treated for the most part by Mint Water*', and 'Remarks on the Natural History of Rheumatic Fever', *A Collection of the Published Writings of Sir William Gull*, New Sydenham Society, 1894.

the body is competing with a vast invasion of living organisms, it can scarcely be regarded as a sound principle to inoculate it with a few more millions of dead organisms; in practice I have never yet been assured of resultant benefits. Nor have I seen good done by injections of eusol or mercurochrome in cases of septicaemia, or been persuaded by the literature of the subject that the happy results which sometimes followed the treatment were due to it. Again, on the score of reason, it seems at least unlikely that a small amount of antiseptic, further diluted in many pints of circulating blood, will materially influence a thriving blood-stream infection. A successful chemotherapy for bacterial disease, it is now shown, must be based on other principles than simple antisepsis. There is one further objection to the use of pseudo-specific therapies, and that is that they are apt to impart, at a time of necessary anxiety, a sense of security, a feeling that 'something is being done', thereby leading at times to a neglect of elementary, but none the less important and better proven, measures of treatment. Of his own expectant, observant method Gull truly remarked, 'It required often more consideration than was requisite for prescribing any supposed appropriate drug treatment.' Sulphonamides were only a little more encouraging than other chemical treatment in the staphylococcal fevers, but penicillin has now established its benefit beyond dispute.

The general principles of non-specific treatment in staphylococcal fever may be briefly summarized under three headings: (1) good nursing, (2) a copious fluid intake of at least six pints of fluid in the twenty-four hours for an adult, and (3) watchful clinical care for metastatic abscesses and considered judgement which to open and when to open them. Osteomyelitis once called for early operation, but penicillin has made drastic and early intervention less necessary. An established perinephric abscess should be dealt with without delay. The loin may sometimes be incised with advantage in perinephritis even though no pus be found. Abscesses in skin and muscle should be opened when 'ripe'. The pulmonary abscesses are better left to themselves. Pleuritic fluid may be aspirated. Should a stage of weakness and low

fever without organisms in the blood-stream follow upon an acute septicaemic phase, sunshine and fresh air are invaluable adjuncts to treatment. Even a slight persistent pyrexia should, however, suggest the possibility of a hidden abscess and the body should be searched systematically with a finger-tip in likely regions for any tender point or points. If there is any suspicion of a focus in bone, a careful radiological examination is also necessary. Sir Charles Symonds once described to me a case of staphylococcal septicaemia complicated by cervical root pains and some dysphagia. Later, when the septicaemia had subsided, convalescence was retarded by continued low fever. Eventually a second set of radiograms of the neck was taken, revealing extensive destruction of the fourth cervical vertebra by osteomyelitis, in spite of which the patient had retained free movements of the head and neck.

Summary

Staphylococcal infections of the skin are complicated from time to time by a blood-stream invasion. This may take a benign form (bacteriaemia) and produce a single 'fixation' metastasis, or several small abscesses without real danger to life. Alternatively there may result a severe form (septicaemia or pyaemia) with prolonged fever, rigors, sweats, multiple metastases, and positive blood cultures. The favourite site of localization in adult life is the renal cortex, usually with secondary perinephritis or perinephric abscess. Other tissues frequently involved are the lungs, the skin, the muscles, and the prostate gland. Brain abscess is a rare and grave complication. The differential diagnosis from streptococcal fever is made by the tendency to the development of multiple abscesses in the tissues named; the absence, as a rule, of infection in joint cavities and other cavities lined by serous membranes (excepting when infection spreads from the lung to the pleura or from bone to joint); the absence of glossitis, diarrhoea, and progressive anaemia; the relatively slow pulse; and by blood culture.

Lung-complications with haemoptyses and profuse sweats may lead to a faulty diagnosis of pulmonary tuberculosis.

Perinephritis or a vertebral metastasis may lead to a diagnosis of spinal or hip disease. Prolonged initial fever without obvious metastases may lead to a diagnosis of typhoid fever, but the sweats, the rarity of splenic enlargement, the absence of rose-spots, the leucocyte count, and a blood culture help to establish the correct opinion. In both diseases the pulse tends to remain slow at first. In every case of obscure continued fever a careful inquiry should be made in regard to recent carbuncle or furunculosis, or, in fact, to any history of local skin infection at any time in the previous three to six months. With youth and a good leucocytosis the prognosis in staphylococcal septicaemia is by no means bad. With penicillin, watchful care, good nursing, a copious fluid intake, surgical treatment of abscesses which can be readily approached, and sunshine and fresh air in convalescence, there is n good prospect of complete recovery. The early appearance of a natural fixation abscess is a favourable feature. Vaccine therapy should be avoided at all stages. Drastic surgical intervention has now become much less necessary, even in cases with bone infection.

XVII

THE NATURAL HISTORY, PROGNOSIS, AND TREATMENT OF STREPTOCOCCAL FEVER

In the previous lecture an attempt was made to portray the essential clinical features of generalized and metastatic infections with *Staphylococcus aureus.* It was shown that the primary focus was usually to be found in a boil or other superficial skin lesion and that, although the sequels of a blood-stream invasion were very varied, certain symptomatic and historical peculiarities made it convenient to review staphylococcal bacteriaemia and septicaemia (together with renal carbuncle and osteomyelitis) under a single heading, regarding them collectively as the manifestations of a specific fever.

The same treatment is possible in the case of streptococcal bacteriaemia and septicaemia, but here we are confronted with greater difficulties of presentation because the strains of streptococcus capable of causing blood-poisoning are many and the possible routes of invasion numerous, the natural course of the disease being much influenced by these and other factors. Scarlet fever, erysipelas, puerperal fever, and, in most instances, infective endocarditis, are streptococcal fevers, but it would clearly be unsound to confine them within a single category. The natural history of the diseases named and the bacterial strains involved separate them from each other far more widely, for instance, than the individual members of the typhoid group are separable. Furthermore, scarlet fever and erysipelas may themselves be complicated by a streptococcal septicaemia clinically comparable with the 'surgical' and 'obstetric' septicaemias, and yet not to be considered as an essential part of the primary disease. Epidemic influenza may also be complicated by a streptococcal septicaemia, and the merging of the two diseases creates a clinical picture unlike that produced by either disease alone. A terminal streptococcal

septicaemia is not rare in severe debilitating diseases, and particularly in those marked by a grave anaemia; here the septicaemia is merely an incident due to an invasion of tissues deprived of their proper nutriment and resisting powers.

These difficulties notwithstanding, it is possible to select cases illustrating types of streptococcal fever sufficiently distinct in their clinical behaviour and pathology to warrant separate consideration. Whether from the point of view of diagnosis, prognosis, or treatment, such separate consideration is useful. Once more, as with the staphylococcal cases, we may draw a useful distinction between streptococcal bacteriaemia and septicaemia. The term streptococcal fever is intended to include both. It is employed partly to foster the analogy of a specific bacterial disease or a group of specific bacterial diseases, and partly to avoid a certain ambiguity which attaches to the word septicaemia. Do we in using it distinguish sufficiently between a condition in which organisms are finding their way into the blood-stream and may occasionally or momentarily be demonstrable there, and one in which they are actively thriving and multiplying in the body fluids? The anxiety engendered by a laboratory diagnosis of septicaemia becomes greatly mitigated when clinical judgement can insist that a particular case exemplifies the former rather than the latter event. On the other hand, can we always exclude as non-septicaemic cases which have all the clinical characters of a septicaemia, but which give negative cultural results? On the analogy of typhoid fever and infective endocarditis we cannot do so, for in these diseases there is a considerable percentage of cases in which blood cultures remain sterile. For the diagnosis of bacteriaemia and septicaemia we must ever require a proper balancing of all the available evidence whether obtained at the bedside or in the laboratory.

In this paper it is proposed to consider with illustrations (*a*) the aetiology and paths of invasion; (*b*) the outstanding clinical features and differential diagnosis; (*c*) the prognosis; and (*d*) the treatment of streptococcal fevers other than scarlet fever, erysipelas, and infective endocarditis.

(*a*) Aetiology and Paths of Invasion

Age and sex would seem to have little or no influence on the incidence of streptococcal fever if we exclude the puerperal cases. Season has its influence only in so far as it helps to determine epidemics of influenza or of the exanthemata or throat infections commonly complicated by sinus inflammation and middle-ear disease. Fatigue may play a part, and it is commonly held that the overworked surgeon in need of a holiday is more liable to fall a victim to grave sepsis than one in happier circumstances. Exhaustion such as obtains after a difficult labour may be reasonably regarded as a factor in puerperal fever, although it can scarcely be said to operate except in concert with other factors such as anaemia and local trauma. If surgical injuries be excluded, the most apparent causes predisposing to streptococcal fever are (1) other infections, and (2) anaemia. Influenza, scarlet fever, measles, and staphylococcal infections, whether local or general, may all pave the way for a streptococcal invasion. Grave anaemias, as has been mentioned, may terminate fatally with a streptococcal septicaemia which is usually brief in its course and masked by the symptoms of the antecedent disease.

While staphylococcal fever originates in some surface lesion of the skin such as a boil or carbuncle, streptococcal fever may date its inception from an invasion of a cutaneous or a mucous surface or deeper structures, and may occur without an evident local focus. Wounds so trivial as a needle-prick or a hang-nail may provide the portal of entry for a virulent infection and determine a septicaemia as devastating in its consequences as one acquired through a severe war-wound or the placental site. The following list, without pretensions to completeness, indicates the wide variety of causes, sites, or modes of infection which may be encountered: (1) a needle-prick or hang-nail, particularly in the case of surgeons, nurses, and morbid anatomists; (2) any punctured wound or laceration; (3) a corn infected by injudicious paring; (4) a mosquito-bite; (5) an infected haematoma; (6) a tonsillitis; (7) a throat infection in patients from whom

the tonsils have been removed and sometimes in that event with little or no local soreness or redness; (8) a middle-ear infection with, or more rarely without, evident mastoiditis or lateral sinus thrombosis; (9) infection of one or more of the accessory sinuses; (10) an infected tooth socket, without or following extraction; (11) the uterus after a confinement or abortion; (12) an acutely inflamed viscus with peritoneal infection. A skin infection may lead first to a whitlow or to a local or spreading cellulitis, to a lymphangitis, or to a suppurative adenitis, or alternatively without any contiguous spread or evidence of active co-operation on the part of the natural lymphatic barriers, a small red spot or local lymphangitis is succeeded by a rigor and a rapidly developing septicaemia. Given a virulent infection the less the lymphatic defences are called into play the greater, of course, is the likelihood of a grave general infection. In some fulminating infections, whether originating in a cutaneous wound or a throat infection or elsewhere, it would thus seem that the organisms pass directly into the circulation and that the lymphatic system has been 'caught napping'. In the particular case of the surgeon and the pathologist we may sensibly argue that the virulence has been recently increased by 'passage'.

(*b*) Outstanding Clinical Features

Rigor or high fever with chilliness and malaise is the first manifestation of streptococcal fever. Repeated rigors are perhaps more frequent in streptococcal than in staphylococcal fever, and this may be correlated with a lesser tendency to the formation of spontaneous fixation abscesses in the former. In the graver cases the temperature rapidly soars to 104° or 105° or even higher, and death may ensue within a few days or even within twenty-four hours. In cases which survive the initial onslaught the temperature maintains a general high level at first with considerable diurnal oscillations. In the more chronic cases and stages there is a regularly remittent or intermittent pyrexial curve such as is also seen in streptococcal infective endocarditis. Charts A and B (pp. 241, 242) illustrate the first three weeks and a

period of three weeks shortly before the final defervescence in a severe case of septicaemia due to a haemolytic streptococcus (Case 2). The total period of fever was here about twelve weeks. With the stage of high fever go delirium, prostration, restlessness, sighing, vomiting, a dry, red tongue, and splenic enlargement. The spleen may enlarge very rapidly and considerably, but at first it is so soft as not to be readily palpated. This is explained by the fact that in fatal cases the spleen pulp at necropsy is found to be almost diffluent. High fever, rigor, delirium, and prostration can proclaim any septicaemia, but there are four manifestations which may be regarded as peculiarly diagnostic of streptococcal fever and as expressing, I believe, infection with a haemolytic strain. These are: (1) diarrhoea, often frequent and troublesome; (2) the presence of albuminuria with red cells and casts in the urinary deposit and occasionally a smoky urine; (3) rapidly progressive anaemia; and (4) a smooth, red, desquamated, and sore tongue. Some or all of these findings are common in puerperal septicaemia, which is so often due to a haemolytic strain, but I have seen them just as manifest in other cases, and first became familiar with them while in charge of chest-wounds during the 1914–18 War The diarrhoea of puerperal septicaemia is commonly attributed to the local peritonitis, but as it occurs also in non-peritonitic cases, this requires qualification. A representative case under the care of Sir Arthur Hurst, previously reported by me in the *Clinical Journal*, April 1922, may be requoted here.

Case 1. Charlotte I., aged 23, and married, was admitted for pains in the right buttock and diarrhoea on 20 February 1920. Five weeks previously she had had an attack of 'tonsillitis and influenza'. Three weeks later she had a double quinsy, which was opened. On 22 February she developed uncontrollable *diarrhoea* and vomiting. The next day symptoms persisted and she had sharp pain in the right buttock and pain on moving the right leg. On admission her temperature was 104°, pulse 122, respiration-rate 20; cheeks flushed; tonsils large and red; the spleen just palpable. *The urine contained albumin, red cells, leucocytes, and granular casts.* Leucocyte count 12,000 cells per cub. mm. on 27 February. There was tenderness over the sacro-iliac joint. Cultivations from the urine were sterile. From the faeces *B. coli* and *Streptococcus longus* were grown; from the throat *Micrococcus*

catarrhalis, *Staphylococci*, and *Streptococcus longus*. On 7 March blood cultivations grew *Streptococcus longus*. Between 12 and 18 March 120 c.c. of polyvalent anti-streptococcus serum were given intravenously, and two rigors were recorded. On 20 March, although the temperature at the time was 101°, blood cultivations were negative. On 31 March albumin having disappeared from the urine some days previously, both legs suddenly became oedematous without signs of venous thrombosis. The oedema soon subsided, the temperature fell by lysis, and the patient was discharged well on 9 May. No local developments calling for surgical intervention were recorded. The serum, which was administered late, as the infecting organism was not at first determined, produced no striking effect on the pyrexial curve.

The special manifestations described above are perhaps an index of the highly cytolytic properties of the bacterial toxins elaborated by haemolytic strains. It is reasonable to suppose that both the nephritis and the entero-colitis are due to a toxic rather than a local bacterial action, sustained by the kidneys and bowel in their attempt to excrete these poisons. In favour of this supposition I can quote a case of streptococcal fever in which these special symptoms were present, resulting from a local *pelvic peritonitis* without septicaemia, with a negative blood culture, and showing rapid recovery after local surgical drainage.

The pulse-rate in streptococcal fever is rapid from the beginning, when figures of 120 and upwards are commonly recorded. In the absence of lung complications the respiratory rate is not considerably raised, a useful distinction from the pneumococcal fevers. Various rashes—scarlatiniform, morbilliform, or a blotchy erythema, and more rarely petechial haemorrhages—may appear within the first few days, and are usually transitory. Icterus may complicate the haemolytic infections. Venous thromboses occur as in other septicaemias. In cases which survive the first few days there is generally a leucocytosis varying from 12,000 to 30,000 cells per cub. mm. The haemoglobin in the haemolytic infections falls rapidly to figures as low as 20 or 30 per cent. Apart from haemorrhage and the acute leukaemias there are probably no diseases in which a severe secondary anaemia develops so abruptly. The diarrhoea is not as a rule accompanied by the passage of blood and

mucus. The nephritis is usually transient and not accompanied by signs of renal inadequacy. Emaciation takes place with great rapidity in the graver cases. A lobar pneumonia may also complicate a streptococcal invasion. When such a pneumonia is accompanied by anaemia and is slow to resolve, lung puncture will probably give a haemolytic streptococcus. Although delirium has been mentioned as an early symptom, there may be a quite remarkable mental acuity. Trousseau gives a vivid description of this in his account of the puerperal cases, contrasting it with the grievous physical plight of the poor victims. He also lays emphasis on diarrhoea as a leading symptom.

A streptococcal septicaemia may run its course to death or recovery with or without metastatic symptoms. The favourite localizations are in cavities lined by serous membranes. The medium or larger joints, the pleural sacs, the pericardium, the meninges, and the peritoneum are affected probably in this order of frequency. R. E. Smith[1] has drawn particular attention to the close simulation of a true infective arthritis by peri-articular inflammations in the cellular planes.

The clinical diagnosis of streptococcal fever (septicaemic type) may, in brief, be based upon the association of high fever, rigor, quick pulse, delirium or an over-alert mentality, rapid splenic enlargement and metastatic infection of serous cavities. To these may be added diarrhoea, sore tongue, nephritis, and anaemia in some cases of infection with haemolytic strains. A careful inquiry with regard to possible sites of invasion is clearly of the first importance.

The differential diagnosis from staphylococcal fever has been described in some detail in the previous lecture. Suffice it to say that in staphylococcal fever a history of boils or a carbuncle, a slow initial pulse-rate, the liability to the formation of abscesses in the renal cortex and to osteomyelitis are characteristic, and that splenic enlargement and involvement of serous cavities are rare. Pneumococcal fever may also present difficulties. The absence of any primary focus; the hot, dry skin; herpes labialis;

[1] *Guy's Hosp. Reports*, 1931, lxxxi. 1.

and the considerable rise in the respiration rate even in the absence of patent lung signs are among the distinguishing features, but the pneumococcus, although favouring lung, pleura, and pericardium, may also settle in joints and the meninges and, in peritonitic cases especially, can cause diarrhoea.

As always, it is the cases or stages with fever alone and lacking local manifestations that present the greatest difficulties. Here the leucocyte count to exclude a typhoid group infection and blood cultivation, which should ideally be made in every case of obscure and anxious fever, will have their special value.

In streptococcal fever (bacteriaemic type) the constitutional disturbance is less severe, the pulse-rate less soaring, repeated rigors are not observed, and exhaustion and anaemia are less evident, but metastatic infections may equally well occur (*vide* Case 6). Alternatively, the fever may be traced to a localized infection, as in the case of pelvic peritonitis referred to above.

In the case-histories reported hereunder the varying modes of origin and the diverse complications find free illustration, but it may be claimed that a sufficient similarity in clinical course and history becomes apparent in their perusal to warrant the inclusion of all the cases under the single heading of Streptococcal Fever.

Case 2. *Streptococcal Fever (Septicaemia) following a Staphylococcal Infection. Multiple Arthritis. Recovery.* A young married woman, shortly after a confinement, developed a furuncle in the meatus of her left ear. This was complicated by a suppurative parotitis on the same side, the infecting organism being reported as *Staphylococcus aureus*. Three weeks later, when apparently almost convalescent from this but still troubled with a salivary fistula and slight pyrexia, she became suddenly ill and developed a diffuse rash, at first morbilliform, then scarlatiniform, and, when I first saw her, appearing as a diffuse erythema. The temperature rose to 105°; pulse 140; respirations 28. The spleen was palpable and tender. Blood cultures grew profuse colonies of a haemolytic streptococcus within twelve hours. Leucocyte count 24,000 cells per c.mm. On the next day she was worse, with irregular breathing and apnoeic pauses, and vomiting was frequent. On the second day of the illness she was given 40 c.c. of mixed polyvalent anti-streptococcus serum subcutaneously. On

each of the three following days she was given 60 c.c. of mixed serum (i.e. from several big manufacturing firms) intravenously, without apparent benefit. Rigors occurred at intervals during the first week (*vide* Chart A). On the fifth day effusion occurred into a knee-joint, and was aspirated then and on the seventh day. At a later date the *joint was drained. Other joints became inflamed and swollen, but* later subsided. Liberal fluids, glucose, and alkalis were given by

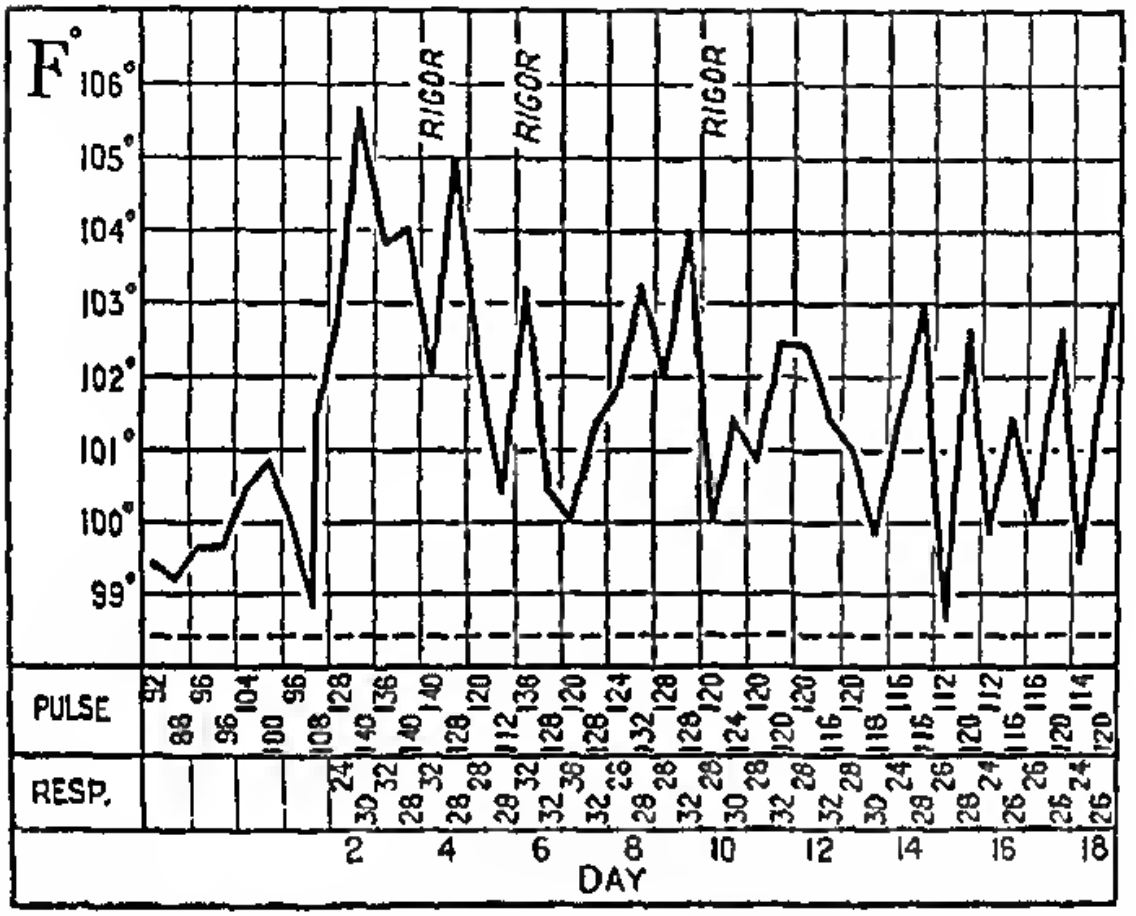


CHART A. Initial phase.

mouth, and glucose with saline per rectum. Omnopon was given at night for pain. The total duration of the fever was twelve weeks. Latterly emaciation was very marked, and there was a continued low-grade pyrexia. At this stage she was seen by Lord Horder, who discovered a tender point in the muscles above the infected knee. A small abscess here was drained, and thereafter the temperature soon returned to normal and convalescence was not seriously interrupted. With the exception of a partially stiff knee, recovery was complete. Expert and devoted nursing, a copious fluid intake (even at the height of her illness this patient took from six to eight pints of milk in the day as well as other fluids), and timely surgery impressed me as the most serviceable elements in the treatment.

CASE 3. *Streptococcal Fever (Septicaemia) complicating Influenza. Frontal Sinus Infection. Hyperpyrexia. Death.* A male worker in a

sweet factory, where he had been working overtime, developed a cold on 8 December 1925. During the next two days his letters home were reported as 'strange'. On 10 December he was seen by Dr. A. H. Elliott, with headache, generalized pains, and a temperature of 102°. A blotchy rash was also noted in the groins and extending down the legs. On 12 December I was asked to see him. He was delirious, truculent, and would not stay in bed, which, he declared, was occupied

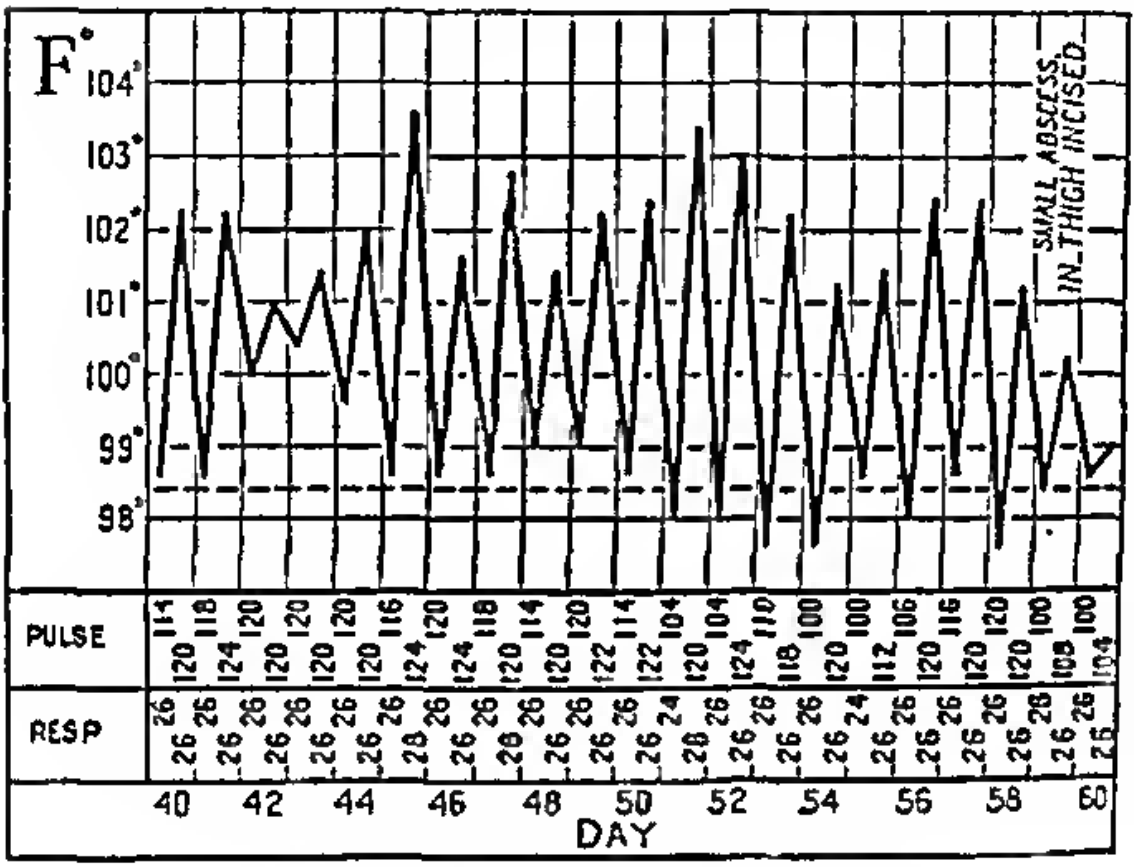


CHART B. *Phase preceding final defervescence.*

by someone else. It was very difficult to examine him. His tongue was coated with a yellowish fur; throat very red, with a film of muco-purulent exudate; slight oedema around left orbit; pulse 120; rapid breathing, but no distress; his feet had a curious purplish colour when he sat up; the spleen was not palpable; and there were no pneumonic signs. He was sent into hospital, and was very violent on arrival. His temperature rose to 108° in the axilla and he died the same night. I diagnosed influenzo-streptococcal septicaemia, and on the analogy of cases recorded in the 1918–19 epidemic suggested that pus would be found in the sphenoidal cells at autopsy. This was the only thing found, with the exception of a large soft spleen and some pus in the gall-bladder. Blood cultures and the pus both grew a non-haemolytic streptococcus. *Streptococcus viridans* was grown from the cerebro-spinal fluid and the heart's blood.

CASE 4. *Streptococcal Fever (Septicaemia) following a Surgical Wound. Lymphangitis. Cellulitis. Spleen Tumour. Recovery.* A medical man, aged 28, had been feeling tired and out of sorts. On 9 October 1928 he performed an operation for adenoids on a child whose father had recently had a bad tonsillitis. He barked his knuckle on an instrument. By the next morning his temperature was 103°, he felt and looked very ill, and had a line of lymphangitis spreading up the arm. There were no enlarged glands. He had a pain in the left lower chest and was very restless when I saw him on the evening of 10 October. His pulse varied from 110 to 120. He was sweating profusely. I felt very anxious about him, and gave him 10 c.c. of scarlatinal antitoxin with 30 c.c. of polyvalent antistreptococcic serum intravenously. Half an hour later he had a bad rigor, and then, after morphine, passed a good night. On the next day he was distinctly better, with pulse-rate down to 100. I saw him again on 13 October. The temperature had risen again to 102°, but the general condition continued to improve; much swelling of dorsum of hand; lymphangitis of arm less evident; still complaining of discomfort at the left rib margin, especially on sitting up. I thought I could feel the spleen. I saw him again on 20 October with Dr. W. M. Erskine, Dr. H. A. Watney, and Mr. E. C. Hughes, his improvement having been interrupted by further pyrexial spikes and some fresh lymphangitis. Except in the pyrexial attacks, however, his pulse did not exceed 90 to the minute and appetite was good. The spleen was now large and firm, and extended three fingers down on inspiration. The history, the appearance of this patient on the first day, and the subsequent great enlargement of the spleen (no other non-tropical fever causes such rapid enlargement) were eloquent of a streptococcal septicaemia. The general impression of the patient and his medical advisers was that the septicaemia had terminated after the administration of the serum, and that the subsequent disturbances were adequately explained by the local sepsis. The case was seen in the country and facilities for blood cultivation were not to hand. Complete recovery followed.

CASE 5. *Streptococcal Fever (Septicaemia) following Difficult Labour and Manual Removal of Placenta.* A woman between 30 and 40 years of age was confined for the first time. She had previously been anaemic and unfit. There was an instrumental delivery after three days of pains, and the placenta was removed digitally. That evening she had a temperature of 104° and a slight rigor. Four days later she was seen by an obstetric surgeon, who found the uterus soft and enlarged up to the navel, feared septicaemia, and put a catheter and glycerine into the uterus. Scarlatinal antitoxin (10 c.c.) was also given. Diarrhoea, which had been troubling her slightly, became profuse, the pulse-rate rose to 120, and I was asked to see her in consultation on the fifth or sixth day. There was considerable

abdominal distension, the spleen was not felt, the uterus was smaller. The leucocyte count was 21,000—a figure which, in the absence of an abscess or pneumonia, suggests septicaemia. Haemoglobin 44 per cent. The diarrhoea was abating and there was slight general improvement. A further dose of antitoxin was given, and a few days later a blood-transfusion. *Except for some transient signs of local* peritonitis in the right lower quadrant, there were no further complications, and recovery followed.

Case 6. *Streptococcal Fever (Bacteriaemia), following Tonsillitis and Cellulitis in the Neck. Arthritis of Elbow. Anaemia. Ambulatory Case.* A man, aged 61, was sent to see me on 14 March 1929. One month previously he had had a sore throat, and then one day at business felt very chilly. He went home, and was there treated by Dr. F. J. Aldridge for a brawny swelling in the right side of the neck which made swallowing very difficult. Pyrexia lasted only a few days, and with poultices and potassium iodide the swelling subsided. Thereafter he kept about, did not avail himself as he should of medical advice, and went for drives, but felt ill all the time. Two weeks later he developed a swelling on the inner side of his left ankle, and a week later pain and swelling in the left elbow-joint. His weight, normally 10 st. 6 lb., had dropped to 8 st. 10 lb. He was pale and slightly dyspnoeic with the effort of undressing. His pulse was very rapid. There was one septic tooth stump in the upper jaw with a cavity exuding pus. Haemoglobin 50 per cent.; leucocyte count 10,650 per c.mm. There were definite signs of fluid in the left elbow-joint, which was tender and resistant to free movement. There was a painless, fluctuating swelling below the left internal malleolus. Infection started in the throat. Anaemia and joint infection (unless as a complication of neighbouring osteomyelitis) are rare in staphylococcal bacteriaemia. I therefore suggested a diagnosis of streptococcal bacteriaemia with metastatic joint infection and advised admission to hospital. The subsequent history of this case has not been obtained.

Case 7. *Streptococcal Fever (Septicaemia) complicating an Osteomyelitis of Tibia. Empyema. Recovery. In the latter half of March* 1929 a young man, aged 18, developed an inflamed area over his right shin. This was incised as a cellulitis. Although he felt well in himself and was afebrile, the wound was unsatisfactory and was twice reopened. On 7 April his temperature rose suddenly to 103° and he had a rigor. Thereafter his temperature remained high and he presented all the appearances of a septicaemia. Cultures from the wound, which was being treated with eusol, remained sterile, but a streptococcus was grown from the blood. Radiograms of the leg showed a central necrotic area in the tibia. Mr. L. Bromley operated, removing necrotic, semi-purulent material. *I was asked to see the patient* with Dr. H. O. Long and Mr. Bromley on 14 April. For the past three days he had suffered intense pain in the right lower chest and

right shoulder, and was looking alarmingly ill. Pulse-rate 120; dyspnoea; orthopnoea. No spleen tumour. No diarrhoea. A large effusion was located at the right base. Leucocyte count, three days previously 16,000 cells per c.mm., had risen to 25,000 cells per c.mm. He had received two injections of polyvalent serum and two of scarlatinal antitoxin and one dose of mercurochrome intravenously. Preparations were being made for an immuno-transfusion. In view of the definite chest localization, the absence of any further septicaemic signs, and the good leucocytosis, I advised against any further serum, chemotherapy, or immuno-transfusion. Needling of the chest to determine the nature of the fluid was performed on 16 April, 8 oz. of turbid fluid being withdrawn. On settling, this showed about one inch of pus at the bottom of a full test-tube. General condition satisfactory. Fluids taken well. Several more needlings were carried out, and each time the sediment of pus on standing showed a definite increase. On 23 April a portion of the ninth rib was resected by Mr. Bromley, and one and a half pints of very thick fluid with flakes of pus were discharged. Treatment with closed drainage. Recovery was slow and tedious, drainage at first not very satisfactory and the wound margin became infected. In September a secondary operation for a persisting sinus was performed, and the patient was subsequently restored to health. The nature of the original osteomyelitis remains undecided, but the history suggests that this case may have been another example of a streptococcal superimposed upon a staphylococcal infection.

Case 8. *Streptococcal Fever (Septicaemia) following an Infected Abrasion. Death.* A hospital sister, aged 40, returned from a holiday feeling in the best of health on 4 June 1929. She was then employed in a very heavy ward with septic cases. On 11 June she had a hot bath, feeling very tired, and almost immediately began to feel ill and feverish, but had no rigor. She developed severe pain in the right shoulder and down the arm, and later pains in the left arm and both legs. On 12 June her temperature was 103°, and chemosis of both eyes with punctate haemorrhages in the lids appeared. There was occasional sickness, but no diarrhoea. Large raised erythematous patches on both forearms, slight epistaxis, and a feeling of tightness in the chest were among the other symptoms noted. I saw her on 14 June, and found her very ill, with dry, dusky red pharynx and blood trickling down from the post-nasal space. There was also a tiny pustule near the nail bed of the right forefinger, where she had experienced slight soreness two days before the onset of her illness. There was no adenitis or lymphangitis. Blood cultures grew streptococci. Leucocyte count 15,000. Scarlatinal antitoxin was given. Death occurred a few days later.

Case 9. *Streptococcal Fever (Bacteriaemia) following an infected Haematoma. Recovery.* A fine, vigorous, healthy M.F.H., aged 64,

bruised his left leg while riding through a gate, paid no attention to the injury, and went to a point-to-point meeting on the next day. Extensive bruising with superficial blebs developed, and these were opened. Deeper planes became infected, and the wound was treated with B.I.P.P. He would not rest properly, and some superficial sloughing occurred. About sixteen days after the injury he felt seedy and had a solitary rigor. Streptococci were grown from the wound and the blood-stream. There was some vomiting, and he had pain after food. The temperature hovered between 102° and 103°, but the pulse-rate was not proportionately raised, there were no further rigors, and he had no diarrhoea. Some cellulitis around the wound and lymphangitis in the groin were next observed. I was asked to see him in consultation with Dr. F. C. Young and Mr. J. L. Joyce at the end of the third week from the injury to advise in regard to prognosis and the treatment of his general condition. He was low and depressed, but had a good pulse not exceeding 80 to the minute, his skin was cool and the spleen was not palpable. Leucocyte count 10,300. I concluded in favour of a bacteriaemia, and for this reason gave a favourable prognosis, and advised against serum therapy or chemotherapy. He had a slow convalescence in respect of the local lesion, but made a good recovery.

CASE 10. *Streptococcal Fever (Septicaemia) following a Throat Infection and Mastoiditis. Septic Arthritis of Hip. Recovery.* A previously healthy little girl, aged 10, had her tonsils enucleated in the middle of March 1930. Just after her return home a virulent streptococcic sore throat affected all the members of her household, including herself. She developed a left otitis media and mastoiditis for which a radical operation was performed. General septicaemia with swinging pyrexia, occasionally as high as 105° and 106°, with rigors, followed. There was also meningism, but the C.S.F. was clear. She was given antistreptococcic serum intrathecally, subcutaneously, and rectally. The spleen became enlarged, and I was asked to see her with Dr. H. E. Rawlence and Dr. C. Picken on 13 April 1930, ten days after the mastoid operation. I found her morale good, her tongue clean and moist, and she was taking fluid nourishment and sleeping well. The spleen was nearly three fingers down and firm, almost hard (compare Case 4, in which by the time the spleen was large and hard the grave septicaemic phase had passed). Pain had just appeared in the left knee, and I found swelling around the left hip-joint which was very painful to move. On 15 April pain in the hip had greatly abated and she was rather better. I was called to see her again on 28 April. The pyrexial curve had adopted a lower level, but the child had become very wasted and anaemic. Spleen smaller. In the last forty-eight hours the left leg had become swollen, an evident 'white leg'. There was some glossitis. On each occasion I ventured a good prognosis as regards life. At this time the haemoglobin was down to 30 per

cent. and the white count was only 9,500 cells per c.mm. A little later the left hip was again discovered to be painful, and X-ray examination, which had revealed no abnormality in the early stages, now showed some destruction of the head of the femur. A plaster 'spica' was applied. The general condition subsequently improved steadily, but the prospects of full functional recovery in the joint seemed poor.

CASE 11. *Streptococcal Fever (Septicaemia). Meningitis. Death.* A girl, aged 13, with a history of otitis media and mastoiditis following tonsillitis three years previously. For this a radical mastoid operation and later tonsillectomy had been performed. Thereafter she enjoyed good health until 19 May 1939, when, in the course of an epidemic of tonsillitis at her school, she was taken suddenly ill with high fever. The temperature reached 105° on the first day. There was no complaint of sore throat and no visible pharyngitis, no cervical adenitis, no splenic enlargement, and during the first three days she was very little inconvenienced by her high pyrexia. On the third day a streptococcus, haemolytic but described as 'not strongly so', was grown from the blood. She was given 10 c.c. of scarlatinal antitoxin, and on each of the three ensuing days 15 c.c. of polyvalent antistreptococcic serum. Her temperature then fell suddenly to subnormal and her pulse-rate from 110 to 76. Two more doses of polyvalent serum (15 c.c.) were given, each time intravenously. On the next day the temperature rose again as suddenly to 105° and the pulse-rate to 120 and 130. I was asked to see her at this point, on the seventh day. In the past twenty-four hours she had developed left-sided headache and a droop in the left upper eyelid. She was clear mentally, had a clean tongue and a moist skin, but was very gravely ill. The most disconcerting findings were a very slight neck-rigidity and Kernig's sign. There were no symptoms or signs of middle-ear disease. On the eighth day the temperature was 105·4°, respirations 30. I advised against any further serum therapy. Lumbar puncture on the tenth day gave slightly turbid fluid under increased pressure. Blood culture now sterile. Leucocytes only 7,500 per c.mm. with 80 per cent. polymorphonuclear cells. Serum given intrathecally. On the eleventh day signs of a right hemiplegia appeared, becoming complete on the twelfth day, when coma and Cheyne-Stokes breathing were recorded and death closed the scene.

(c) PROGNOSIS

Death occurred in one-third of this small series, in one case on the fourth, in one on the seventh, and in one on the twelfth day. It may be generally accepted that those patients who survive the first onslaught and weather the first fortnight have a very fair prospect of recovery even when high pyrexia continues and complications ensue.

Within the first fortnight, in other words, it is commonly decided whether the fight is to be a winning or a losing fight, and whether the infection is to be driven from the general circulation into local strongholds. If the infection is massive or resistance poor, exhaustion or some grave complication such as pericarditis or meningitis will probably prove fatal before two weeks have passed. If the infection is less heavy or resistance good or at least more evenly weighted against the invader, the general defence mechanisms will have been mobilized by this time. By this time too metastatic infections, which sometimes improve prognosis rather than otherwise, will be making their appearance. In two of the three fatal cases described there was no evident focus of invasion. In two no evident metastasis occurred. In the third the very fatal complication of meningitis was the cause of death at a time when organisms were no longer recoverable from the blood. All three patients were young. One was probably infected initially by influenza; one was a sister in charge of a heavy septic ward; the third acquired a rapid general infection through the throat during a school epidemic of tonsillitis and established no lymphatic defence. Cases 10 and 11 remind us of the occasional disadvantage of being deprived of all tonsillar tissue. In the second and third of the fatal cases the leucocyte counts were respectively 15,000 and 7,500 cells per c.mm. The leucocyte counts in five of the cases which recovered were 25,000; 21,000; 19,000; 10,650; and 9,500. Metastatic fixation in joints occurred in each of the two last with low counts and in the pleura in the case with the highest count.

The following points may be said to favour a good prognosis: (1) a surgically accessible focus of invasion; (2) survival beyond the immediate stage of onslaught, i.e. beyond the first fortnight; (3) a high leucocytosis; and (4) favourable localizations amenable to surgical treatment. Unfavourable localizations are those involving the meninges and the pericardium. Blood-borne infections of the peritoneum are also unfavourable.

It has always been recognized that surgeons' wounds and puerperal septicaemia carry a particularly grave risk. In the

first instance this probably depends on the virulence of the infecting strain, perhaps immediately enhanced by 'passage'. In the second preceding anaemia and exhaustion, the extent and seclusion of the raw infected areas, and the readiness with which infection may be spread and absorbed in the pelvis play their inevitable part, and the infecting strain is all too frequently a haemolytic streptococcus.

(*d*) Treatment

The same general principles of non-specific treatment outlined for Staphylococcal Fever may be held to apply in Streptococcal Fever. They include (1) good nursing; (2) a copious fluid intake up to six pints and more in the day, together with glucose and alkalis during the invasion stage when the heart is severely taxed and febrile acidosis and vomiting are commonly present; (3) watchful care for the development of infection in the cellular tissues, joints, pleura, and pericardium, effusions being treated so far as possible by timely aspirations so long as the fluid remains thin, and by surgical drainage if it becomes frankly purulent. When blood cultures become negative, but the temperature remains high, the search for metastases must be pursued with particular care; (4) morphine for pain, restlessness, and sleeplessness; and (5) appropriate immobilization of infected joints. The older antiseptics by the intravenous route are to be avoided. There is *no* sound evidence, whether experimental or clinical, that they do good. Some of them have undoubted toxic effects. Their administration can be distressing to the patient and they are capable of causing disturbing symptoms. The failure of local antiseptics in infected wounds has long been proved and, surely, in generalized infection general antisepsis is less rather than more likely to succeed. Whether or not the administration of antistreptococcic serum is ever a cause of improvement or recovery is also open to debate. In a given case we have no certainty that the sera available are specific for the particular invading organism. It is not proved that any of the available sera are strictly anti-bacterial. Some of them are, however, reputed to be antitoxic, and note-

worthy among them is scarlatinal antitoxin, upon which good reports have been published from time to time both in scarlet fever and other streptococcal infections. On the whole, we must confess that there was never any strong evidence in favour of the efficacy of serum therapy. It was very generally employed for many years, and had its results been in any way dramatic, there would have been a weightier consensus of opinion in support of it. Anaphylactic symptoms were n frequent and sometimes a grave disadvantage. I have had the experience of being called to a case of serum sickness so severe and crippling as to suggest that the patient had entered on a new phase of the original septic infection for which the serum had been given.

But in any case sulphonamides and penicillin have now abolished the need for the use of antiseptics and sera, and have greatly reduced mortality and diminished the tale of local complications. While the benefits of modern chemotherapy can be no more disputed than the malarial chemotherapies, it is a pity that there are no reliable figures of mortality, end-results, and the incidence of main complications by which to effect comparisons of treatment 'then and now'.

Fresh air and sunshine and appropriate treatment of anaemia as soon as possible after the acute phase is passed continue to play the same useful role which they are known to play in other bacterial diseases.

XVIII

THE NATURAL HISTORY, PROGNOSIS, AND TREATMENT OF INFECTIONS WITH *BACILLUS COLI COMMUNIS*

In the foregoing lectures I have considered the clinical consequences of staphylococcal and streptococcal infections respectively. In each I made it my endeavour, largely on a basis of personal records and experience, to sketch the whole natural history of the disease in question, just as one might depict the natural history of typhoid fever, lobar pneumonia, or any other specific malady. By too much concentration on the local effects, the surgical aspects, or the bacteriological characters of the septic fevers and by a neglect of 'the general view' it seemed to me that we were sometimes liable to a loss of judgement in our approach to the practical problems connected with their aetiology, prognosis, and treatment. Starting with the local lesion or invasion the varieties of general dissemination which may follow, leading on the one hand to a more or less benign bacteriaemia, and on the other to a grave septicaemia or pyaemia, were in turn reviewed. For each of the septic fevers certain sites of election in respect of metastasis or residual settlement are discovered which give character to the disease and are therefore helpful in diagnosis. Thus in the case of staphylococcal fever metastases show a selective affinity for the bones in childhood and for the renal cortex and the prostate in adult life, although we find that they may also appear in skin, muscle, lung, and brain. In the case of streptococcal fever the joints and serous cavities are chiefly involved. These preferences on the part of bacteria for different anatomical sites might well suggest fresh avenues of inquiry to the bacteriologist in his studies of microbic biology. There must be some good reason why the septic organisms show such individual preferences; why the pneumococcus prefers the lung, and the meningococcus the meninges, notwithstanding that both have their portal of entry in the upper

respiratory tract; and why organisms of the typhoid group and the colon bacillus, having entered and left the circulation, prefer to colonize the urinary and biliary passages.

In the present paper I am concerned with the wanderings of the last-named organism when it invades tissues beyond the bowel-wall, and more especially with the clinical features of these invasions.

Infection with the colon bacillus is usually held to imply a simple pyelitis or cystitis. While it is true that the renal pelvis and the bladder are the commonest sites of residual infection, they are by no means the only sites, and it should not be forgotten that the urinary infection is only one episode in the natural history of the disease.

Generalized and metastatic infections with this organism, while prevalent and a frequent cause of acute and chronic ill health, do not carry the serious menace to life which we associate with the septic fevers. Indeed, in the absence of associated pathologies, such as obstructive lesions in the urinary tract or other renal damage, it may be doubted whether they are ever immediately fatal.

Aetiology and Paths of Invasion

It is well known that women are far more predisposed to bacilluria than men, and that pregnancy increases this liability. In my own experience it is particularly the dark and sallow women of hyposthenic habit who are afflicted; that is to say women endowed with the particular constitutional traits which we have come to associate with intestinal sluggishness. It must be relatively rare to encounter the disease in persons of robust physique and endowed with healthy complexions and a regular bowel function. An access of constipation due to pregnancy or illness, abuse of purgatives, and particularly such conditions as fatigue or chill or a menstrual period are often the determining factors. There is a group of cases, with which others must also be familiar, in which young and very recently married women are the victims, independently of a pregnancy. Pyelitis and cystitis may, however, occur at any age. Among children girls are more prone to bacilluria than

boys. Among 53 private cases of pyelitis, cystitis, and bacilluria I have notes of 40 females and 13 males. In men (apart from prostatic disease) I chiefly recollect these infections as a consequence of enforced rest following an operation or of typhoid fever or some other severe illness. Whether in the case of typhoid fever the permeability of the intestinal mucosa is increased by local ulceration, or whether a secondary constipation, a long sojourn in bed, and lowered general resistance are the more to blame it is difficult to say. As pyelitis usually complicates early convalescence, the second view is perhaps the more plausible.

It is commonly agreed that the infection derives from the bowel where the colon bacillus is a normal inhabitant, but various theories have been advanced in regard to the actual paths of spread. These include the theory that organisms ascend via the bladder. While a per-urethral infection in women and girls is a possibility, in the male it is anatomically improbable, and in either sex it seems unlikely that infection should advance 'against the stream' and so attack the renal pelvis. Nor is this the order of events if we may judge by the clinical histories of cases of pyelitis. Ascent by the peri-ureteric lymphatics is another hypothesis and trans-peritoneal infection of the kidney a third and, to my mind, the least probable of all. A typical first attack of pyelitis (or, as I should prefer to call it, of bacillaemia with pyelitis) starts with general malaise, headache, fever, vomiting, chilliness or actual rigor, pain in the loin, and, generally a few hours later, frequency and dysuria. The temperature may rise to 103° or more and the aspect of the patient is that of a general rather than a local infection. Furthermore, there are other organs besides the kidney which may be affected separately or simultaneously, immediately or subsequently. Of these the gall-bladder and its ducts are the most important. Thus clinical observations strongly favour the view that the initial infection is blood-borne and that the urinary and biliary tracts only become involved during the excretion of organisms. The phase of bacillaemia, however, is of short duration, perhaps hours only, and rarely or never days as in the bacteriaemic or septicaemic phases of the

septic fevers. Bacillaemia probably ends when the bacilluria begins. It is not improbable that routine blood cultures in the early stage of high fever and rigor in cases of pyelitis would give positive results. Kidd [1], who has strongly advocated the haematogenous theory, and Panton and Tidy [2] have actually recorded positive blood cultures in a few cases during or near the stage of rigor, but it should be noted that their cases were not uncomplicated cases of pyelitis. If the urinary outflow is impeded (*vide* Case 6) the bacillaemia may undoubtedly persist. It is possible also that re-infection of the blood-stream from the kidney or lower urinary tract may occur. Bacteriaemia, with or without rigor, has been shown by Barrington and Wright [3] to follow operations on the urethra, and is the probable explanation of 'catheter-fever', which closely resembles the prodromal stage of a pyelitis.

The residual infections which succeed the bacillaemia may involve the pelvis of one or both kidneys, the bladder, the gall-bladder and bile-ducts, the prostate gland, or the testicle. Occasionally two or more of these organs are simultaneously inflamed. Where the kidney is concerned it can generally be assumed that the inflammation is confined to the pelvis and calyces, but in the presence of obstructive lesions a pyelitis can proceed to n pyelo-nephritis or a pyo-nephrosis. The cholecystitis also is, as a rule, simple or non-suppurative, and the same may be said of the orchitis. With each organ the natural tendency is to a rapid subsidence of the acute inflammation with rest and appropriate treatment. There is, however, both in the biliary and in the urinary tracts, a strong subsequent tendency to persistent low-grade infection either without symptoms or with vague impairment of health and occasional sharp recurrences. The most severe initial illness may, however, be followed by complete and lasting recovery.

Clinical Features and Course

(1) *The Urinary Infections*

These can best be illustrated by the histories of a few cases of varying type and severity. We may, however, add

to the brief description of symptoms outlined above that there is commonly very considerable malaise and prostration for the first few days; that vomiting and abdominal pain, sometimes with distension, are frequent; that palpation of one or both of the kidneys may give pain, but that there is not usually an appreciable enlargement of these organs; and that micturition, owing to the cystitis, is frequent and accompanied by burning or scalding especially at the end of the act. The urine, when held up to the light and shaken in a test-tube, is seen to be turbid and shimmering. Given a fresh specimen this 'shimmering' is a most useful diagnostic sign in cases of obscure fever or dysuria (*vide* Case 3). In some cases, and especially in the chronic phase and after standing, the urine gives the well-known 'fishy' odour. The reaction of the urine is strongly acid. Albumin is present but usually in slight amount only. Some cases display a frank haematuria for a brief period. The centrifugalized deposit under the microscope shows countless pus cells and organisms. With early diagnosis and appropriate treatment, including alkaline therapy, the temperature declines rapidly by lysis in a few days and only rarely persists for more than a week. Defervescence is commonly complete soon after the urine becomes alkaline. Anaemia is not a feature of bacilluria, but a coexistent anaemia due to another cause may help to perpetuate infection. Relapse and chronic bacilluria will be discussed in more detail under Prognosis.

(2) *The Biliary Infections*

Cholecystitis, with which in the more chronic cases a mild degree of cholangitis and hepatitis are probably associated, is more insidious in its arrival than the urinary tract infections. Subacute attacks with a 'spike' of pyrexia, nausea, right subcostal or mid-epigastric pain and tenderness, and pain referred to the right scapular angle are the common clinical manifestations. To such cases the label of 'gastric influenza' is very commonly applied. Many of the cases are seen between attacks for dyspeptic symptoms, of which nausea, epigastric soreness, and flatulence are the more

prominent. The patients are sallow and pale and they may acquire with the passage of years the muddy complexion which is customarily ascribed to 'intestinal toxaemia', but which may be observed in other varieties of hepatic disease. There may be slight persistent temperatures of 99° or thereabouts. Occasionally a pale stool or loose motions are noted. Jaundice is not frequent, and major biliary colic, unless stones are present, is also rare. The epigastric discomforts have no precise relationship to meals and the nausea is continuous or comes 'in waves' and without a special morning incidence as in gastritis and pregnancy. Examination shows no enlargement of the gall-bladder. There may be slight flinching or guarding on palpation over the right upper quadrant of the abdomen, and tenderness during a deep breath at the gall-bladder point is usual, but varies in degree with the activity of the inflammatory process. Some cases show referred tenderness over the middle dorsal spines. The age incidence of simple cholecystitis lies especially in the second and third decades and women provide the majority of the cases. The physical type afflicted is again the costive, hyposthenic type. By these features it may be distinguished from the stouter and more robust type, with deep chest and broad epigastric angle, which we have come to associate in the fourth or fifth decade with cholelithiasis.

Case Reports

Case 1. *Simple recurrent pyelitis and cystitis.* A young married woman, who gave a history of a short, sharp attack of pyelitis in the seventh month of a pregnancy 8 years previously, was troubled one day with slight frequency and fever. Against advice she did not keep to her bed. Dysuria persisted for a week. She then had a solitary rigor one night and was feverish and chilly throughout the next day. At the time of examination her temperature was 102° (Chart 1); tongue furred; pain in the loins. A period started on the following day. The urine was 'loaded' with pus cells and *B. coli*. With rest, liberal fluids, and copious alkalis symptoms rapidly abated and the temperature was normal by the fifth day of treatment. The urine rapidly became clear of pus cells after this and again after one subsequent slighter attack, alkaline therapy being employed on each occasion. Three years later the patient is in excellent health.

CASE 2. *Acute pyelitis complicating auricular fibrillation. Severe abdominal pain.* A woman, aged 54, had been under treatment for auricular fibrillation with pronounced tachycardia (i.e. complete rest and digitalis) during a period of eleven days. She then complained of a sudden access of very intense abdominal pain which she was unable to locate with any accuracy. There was also a complaint of pain down the left leg, but this was transient. She looked ill and was unresponsive and mentally peculiar. I noted a vague epigastric tenderness but no rigidity and no elevation of pulse-rate or temperature. On the

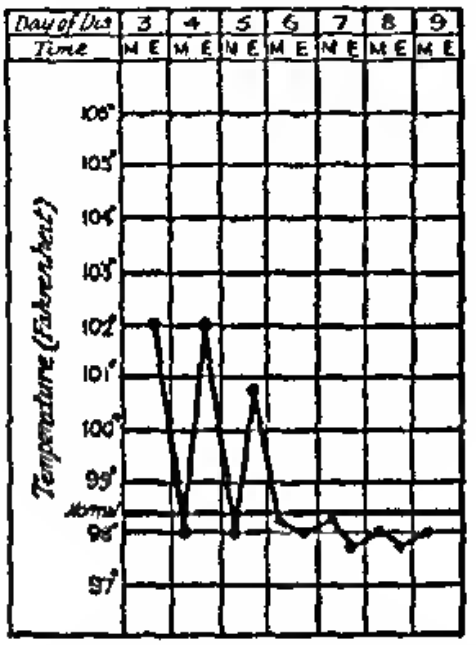


CHART 1

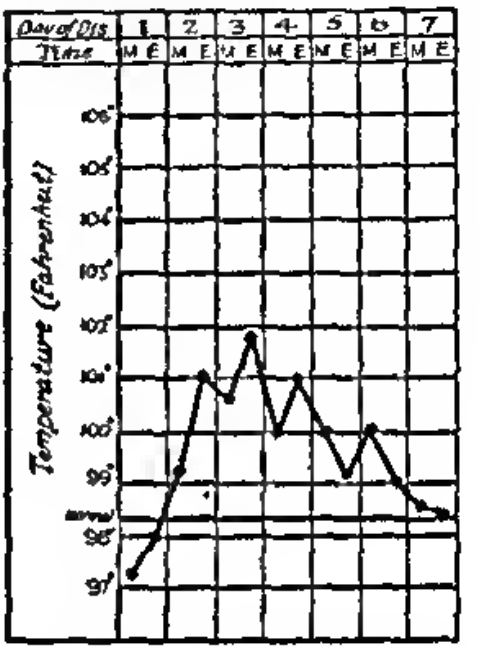


CHART 2

next day the temperature rose to 101° in the evening and there was tenderness below the right rib margin. The urine showed albumin, copious pus cells, with an occasional red cell, and was highly acid. The pulse-rate, which had been recorded at 160 before digitalization and which had fallen to 88, only once rose above 92 during the period of the urinary infection. Alkaline treatment was started promptly with immediate alleviation of symptoms. The course of the fever is illustrated by Chart 2.

CASE 3. *Pyelitis in a child causing obscure pyrexia.* A small girl, aged 4½ years, previously lively and robust and of healthy parentage, had been ill for a fortnight at the time of my visit. The onset of her illness had been abrupt with fever, headache, and vomiting. A swinging pyrexia varying between 99° in the morning and 102° or 103° in the evening had continued ever since. Bowels costive. No chills or sweats. Appetite good. There had been complaint of dysuria on one occasion only and there was no frequency. The physical examination was entirely negative. Tuberculosis and typhoid fever had been under discussion. On shaking a fresh specimen of urine in

a test-tube held against the light typical shimmering was observed and the microscope revealed pus cells and *B. coli*. There was a satisfactory response to alkaline treatment.

Case 4. *Acute cholangitis, pyelitis, cystitis, and orchitis.* A medical man, aged 35, who had been seriously ill with acute nephritis in 1912, but recovered and served through the War, was subsequently explored on account of gall-bladder pain in 1919. He was then well until February 1925, when he became ill with 'influenzal' symptoms and took to his bed with a temperature of 101°. Five days later nausea, vomiting, and jaundice were added to his symptoms. He was ill for a fortnight and was beginning to improve when he developed follicular tonsillitis and a simultaneous dysuria. I saw him with a temperature of 101°, tenderness in the gall-bladder region, a leucocyte count of 21,000 cells per c.mm., and urine loaded with pus cells. He was admitted to hospital, where he lay gravely ill with *B. coli* pyelitis, cystitis, and later orchitis. He showed no response to urinary antiseptics, but improvement followed immediately the urine was alkalinized. He was given vaccines in convalescence. Recovery was complete. The urine became perfectly clear and has remained so since.

The two cases next to be described exemplify effects which may follow when an obstructive factor is added to infection. In the first case (Case 5) medical treatment failed repeatedly to relieve symptoms. In the second case (Case 6) blockage of the ureter by a calculus, in association with bacillaemia and pyelitis, caused a *B. coli* 'septicaemia' with very grave symptoms which were quickly relieved after drainage of the kidney. By the lessons of Case 5 I have twice been enabled to recognize from the history the presence of an additional mechanical factor complicating infection and calling for surgical relief.

Case 5. *Chronic pyelitis; pyonephrosis.* A boy, aged 18, of rather delicate type, had been liable to febrile attacks from childhood. Eight years previously infection of the urinary tract with *B. coli* had been diagnosed and for 3 years he had recurring attacks of fever due to this. He saw various specialists, but never responded to treatment either with alkalis or antiseptics. He was then better for 5 years. A month before I saw him in consultation with Dr. P. L. Richardson he had again become ill. Further consultations had been held before my visit, the diagnosis of *B. coli* pyelitis had again been confirmed by laboratory inquiry, and the usual treatments, including alkalinization, had been advised. So far from improving his condition, treatment actually appeared to make him worse and this alone was so

unusual as to make me suspicious of some added factor. For some days his temperature had been rising to 103°, there were night-sweats, and he vomited frequently. In this illness his pain and tenderness had been confined to the left loin and there was no dysuria—further points in favour of a localized renal trouble. His parents were acutely anxious and Dr. Richardson and I were therefore agreeably surprised to find them radiant on our arrival because the boy had 'quite suddenly improved' at 10 o'clock that morning and his evening temperature was down to 99°. This sudden improvement again suggested to us that something definite and dramatic must have occurred such as the release of a mechanical block. Hitherto deep palpation had been difficult owing to tenderness, but I found the boy so much more comfortable that I was able to palpate freely in the left loin where I convinced myself of a slightly enlarged kidney. I was presented with numerous laboratory reports on the urine all pronouncing in favour of *B. coli* pyelitis, but decided that I would like to take away a specimen with me. We therefore asked the boy to pass water in our presence. As he did so his jaw dropped and he exclaimed, 'I've never passed anything like that before'. The urine, which had been almost clear in the morning, now consisted of thick creamy pus. He had emptied a pyonephrosis. A shell of a kidney was removed later by Sir John Thomson-Walker and he made a complete recovery. It is evident that his failure to respond to medical treatment had, from the beginning, been due to a partial or intermittent obstruction of the left ureter.

Case 6. *B. coli septicaemia with impacted ureteric calculus.* A nervous and highly-strung married woman, aged 35, was referred to me by Mr. Frank Kidd, under whose care she had been for pyelitis, on account of symptoms referable to her colon. She was liable on the one hand to spasmodic bowel pain and on the other to sudden 'chills'. Eighteen months later, on 1 June 1930, she was wakened by bad pain in the lower part of her back, became ill and pyrexial, and complained of pain and frequency. The pain moved to the left side, she had frequent rigors, and the temperature rose to 106° and later 107°. The onset of the illness coincided with a menstrual period. I saw her in consultation with Dr. P. W. James on 11 June. She was mentally strange, in a typhoidal state, twitching, incontinent, and drowsy. The abdomen was soft and flaccid. She was tender in both flanks. She was passing plenty of urine. The leucocyte count was 17,300 cells per c.mm. with 90 per cent. of polymorphonuclear cells. Blood culture gave a pure growth of the colon bacillus. On 14 June Mr. Kidd drained the left kidney which was full of foul pus. At a later operation he removed a stone from the ureter, and she made good recovery.

It is probable, as Kidd [1] has insisted and as has been argued above, that the rigor-stage of *B. coli* infections

represents a true, if transient, bacillaemia. It would seem to require an obstacle to natural drainage to convert a benign bacteriaemia into the graver state which, in virtue of the hyperpyrexia and typhoidal condition, I have here ventured to describe as *B. coli* septicaemia. The distinction between a bacteriaemia and n septicaemia, which must be largely clinical, I have discussed previously.[1]

CASE 7. *Infection of the biliary tract.* A young woman, aged 28, had a long attack of catarrhal jaundice as a schoolgirl. In August 1921 she had a sudden bad abdominal pain while cycling. Pain persisted for a day or two but, when it left her, she remained unwell and was in bed for 8 weeks with almost constant nausea, poor appetite, cold extremities, and an intermittent pyrexia of 99° to 100°. She lost weight considerably, but had begun to improve by the time I saw her. Her doctor had been apprehensive of pulmonary tuberculosis. Of this I could find no evidence. She was sallow and pigmented and the blood-pressure was low. There was tenderness under the right rib-margin during inspiration. I advised dietary measures, exclusion of eggs, and treatment with urotropine. Her health steadily improved. Two years later her weight had increased by more than a stone, but she still had occasional nausea and right sub-scapular pain.

Other cases show more in the way of local and less of general symptoms, and there is considerable variety in the clinical pictures which may be seen in practice. Simple cholecystitis, which is due to the colon bacillus in the great majority of cases, is also probably the commonest organic cause of chronic dyspepsia in women.

DIFFERENTIAL DIAGNOSIS

The diagnosis of bacillaemia with acute pyelitis and cystitis is not, as a rule, difficult. Cases of right-sided pyelitis with severe pain may simulate appendicitis; cases with much fever and few localizing symptoms may suggest a typhoid-group infection; and cases with haematuria may have to be distinguished from renal calculus. A careful history and a macroscopic and microscopic examination of the urine will generally decide. In the chronic phase both pyelitis and cholecystitis may lead to fruitless appendicectomy. The orchitis may be erroneously attributed to

[1] *Vide* Lectures XVI and XVII.

gonococcal or other infection. The general malaise and debility and the slight recurring pyrexia which characterize some of the biliary tract infections may readily create apprehension about early pulmonary tuberculosis, and the pain of perihepatitis in such cases has been attributed to pleurisy. The symptoms of acute and sub-acute cholecystitis are often attributed to 'gastric influenza'.

Prognosis

As indicated above the prognosis in regard to life in uncomplicated cases of bacilluria is uniformly good. Where the infection complicates old age or a paraplegia it may hasten the end. As a complication of ureteric blockage or prostatic enlargement its seriousness has been fully appreciated by the genito-urinary surgeon and, in the latter case, the risks of renal failure are known to be much increased.

The prognosis with regard to full restitution of health is always somewhat uncertain. Many cases, it is true (perhaps the majority), recover completely or, as in Case 1, enjoy long spells of good health. Others retain a permanent bacilluria and a liability to recurrent attacks of pyelitis and cystitis. Others again retain a bacilluria but are well. A young man of my acquaintance has had a pyuria evident to a naked-eye inspection of his specimens for many years but without any untoward symptoms. These chronic bacilluric cases are very resistant to treatment whether with antiseptics, alkalis, or vaccines. The method of treatment with ketogenic diets at one time seemed to offer better prospects of success.

I am strongly of the opinion that if alkalinization were complete and sufficiently prolonged in the first instance there would be fewer cases of chronic bacilluria. Time and zeal are commonly misspent in the exhibition of antiseptics and vaccines.

With the biliary tract infections there is the same liability to relapse and chronicity and the way may be paved for gall-stone formation in later life. Early diagnosis and active treatment should diminish these liabilities, but the symptoms often linger unrecognized for years and long perpetuation

of the local inflammatary process naturally interferes with successful medication.

Treatment

The treatment af acute pyelitis should include bed, warmth, plentiful barley-water, fruit drinks, and weak tea, but preferably little milk. The lower bowel should be cleared with an enema. Full dases of alkalis, in the form af potassium citrate and sodium bicarbanate, should be given and the amounts rapidly increased until each specimen af urine passed turns red litmus-paper blue. Thirty grains of potassium citrate with 15 grains af sodium bicarbonate fourhaurly wauld be a reasonable initial dose, but much more may be necessary, and I have given up ta three or four hundred grains of alkali in the twenty-four bours to a child of ten or twelve before alkalinization was complete. The risk of causing an alkaline intoxication is small. As a rule the temperature drops coincidentally with successful alkalinization and the dysuria is quickly alleviated. It was once usual to follow up the initial alkalinization with a course of urotropine and acid sodium phosphate, but thorough alkalinization alone is very effective and the additional treatment doubtfully so. Vaccines were also employed but should play no part in the treatment. According to Shohl and Janney [4] colon bacilli are inhibited from growing in urine at a pH af 4·6 ta 5·0 an the acid side, and 9·2 to 9·6 on the alkaline side, and the ketagenic diet was at ane time in favaur. Studies by Helmholz and Clark [5] reviewed by Cabat [6] suggest that the pH af the urine may be sufficiently raised by a ketagenic diet to ensure sterilization even when alkaline and antiseptic treatments have completely failed. These aver-rich diets are hard ta tolerate and by some patients cannat be taken at all. In any case sulphonamide therapy far urinary sterilization, following initial symptomatic relief with alkalis has superseded these measures. With milder acute attacks the patient should not be kept too long in bed. The after-treatment should comprise a diet liberal in fruit and fluids and rational treatment for constipation, purgatives being forbidden. Fatigue, exposure

to cold, and the approach of a menstrual period are all liable to initiate a relapse and patients should be warned of this.

When symptoms are resistant to routine medicinal measures and there is unilateral pain, the possibility of an obstructive lesion calling for surgical relief should be carefully considered. I have avoided separate discussion of bacillaemia and bacilluria in pregnancy. The treatment of these cases, although usually conducted on similar lines, may on occasion call for special experience to which I can lay no claim.

If urotropine is of doubtful or secondary value in the urinary infections it may still have a place in the treatment of simple cholecystitis. In these cases a morning dose of Epsom salts before food has been taken; a mixture containing 15 (increasing to 30) grains of urotropine with double the dose of potassium citrate three times a day; a diet rich in fruit and green food and excluding eggs; liberal fluids; prohibition of corsets; and regular exercise—the courses of the urotropine being repeated at intervals for a month at a time—may be rewarded. Hurst recommended much larger doses of urotropine. The urine must be kept constantly alkaline with a view to avoiding a chemical cystitis. Many patients accept the value of the régime and voluntarily return to it in the event of a recurrence of symptoms, but it is difficult to decide how far improvements should be attributed to the urotropine and how far to time and nature and the general regimen. Knott [7] has shown that urotropine is excreted as formaldehyde in the bile and that it may exert therein an inhibitory effect on the growth of organisms. Once again it may be necessary to determine the presence or absence of a mechanical factor in the shape of gall-stones. Surgery should only be sanctioned in simple cholecystitis after a very careful review of the history and objective findings and when medical treatment has been tried and failed.

Summary

The colon bacillus (a normal inhabitant of the bowel), in certain constitutional types and as a result of certain well-

recognized disposing causes, may enter the circulation. A transient bacillaemia results and is followed during the excretion of organisms via the urinary and biliary tracts by pyelitis and cystitis, or by cholecystitis. Orchitis and prostatitis are rarer sequels. Late residual infection of the renal pelvis and bladder or of the gall-bladder and its ducts is common. Adequate treatment with full alkalinization in the early stages of the urinary infections gives satisfactory results. The treatment of chronic bacilluria is less satisfactory, but urinary sterilization with sulphonamides, usually quickly accomplished in cases of short duration, is also effective in those of long standing. A tendency to recurrence, however, may persist. In the early and milder biliary tract infections morning salts and disinfection with urotropine have been held to be effective. In a minority of both the renal and biliary cases medical treatment is rendered unavailing by an added obstructive or mechanical factor, the presence of which can often be appreciated by a careful attention to historical detail and symptoms. In these cases surgical treatment is appropriate.

A wider appreciation of the importance of a healthy bowel and avoidance of the purgative habit would probably do more to diminish the incidence of these prevalent infections than any other single measure.

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follows. We need to know how far it is now incumbent upon us to consider the employment of serum in lobar pneumonia as a routine, or if this is not warranted, how we should select the cases to be so treated. Recognizing that the method calls for experience and considerable technical skill we also need to know whether cases can be adequately handled in the home and, if not, whether they ought to be moved to hospital in face of the belief that, given good conditions, the avoidance of such a transfer generally provides a better prospect of recovery.

It is a main purpose of this communication to seek an answer to these questions. My personal experience of serum therapy in pneumonia is negligible, but I have long been interested in the natural history of the disease, and it was my good fortune to be a participant in the discussion on serum treatment arranged by the British Medical Association in 1932. I have also had the pleasure of meeting several of the leading British and American investigators and of serving on committees which are closely concerned with the problem.

There have been discoveries in the scientific treatment of disease in recent years which have been promptly accepted and universally applied, so apparent and remarkable were their achievements. Of such are insulin in diabetes and liver treatment in pernicious anaemia. The anti-pneumococcal sera, also due to careful scientific studies, are, however, in a different category and for various reasons have produced no such dramatic change in practice. They demand special care and experience for their administration; their preparation is costly; they show a limited specificity; it is very difficult to assess the several causes of symptoms and mortality in the disease which they are intended to benefit; and, finally, this disease has already a high natural recovery-rate. We are not entitled to conclude from this that sera will find no established place in our therapeutic armoury. Rather should we seek to determine the scope and limits of their utility.

Now we cannot discuss the merits of a new remedy unless we have a just appreciation of the natural morbidity

and mortality of the disease which it is purported to relieve or cure. For this reason I must ask attention first of all to the difficult matter of prognosis in pneumonia—that is to say, of pneumonia when left to nature and the nurse. Thereafter, having briefly reviewed the contributions of non-specific therapy and the methods and results of serum therapy, I shall attempt an estimate of the extent to which we should be prepared to modify practice on the basis of the newer knowledge.

Mortality and Prognosis

As has been implied, we cannot claim that we are able to reduce the mortality or alter the morbidity of a disease until we know what its mortality and morbidity are. When, as in the case of pneumonia, these vary in some degree from year to year, very considerably from country to country, and markedly so in relation to age, social environment, individual constitutional factors, and the type of invading organism, our difficulties become very complex. Both the prevalence and mortality of pneumonia in the United States, where the bulk of the work on serum therapy has been done, are more serious than in this country and to some extent our conclusions must be drawn anew.

At present we have hospital figures in England and Scotland which show that the mortality of lobar pneumonia lies somewhere between 10 and 20 per cent. Waterfield [1], investigating the figures at Guy's Hospital over a nine-year period ending in 1930, found a total mortality of 16 per cent. between the ages of 13 and 75 years. One-third of the deaths occurred over the age of 50. There were no deaths between the ages of 15 and 20. We have no exact figures as to the mortality of patients treated in their homes, and I imagine that many more patients in this country are treated in their homes than in hospital. As the graver cases and the poorer cases tend to find their way to hospital and as the act of removal is often undertaken rather late in the disease and is not always beneficial to the patient, it would be reasonable to expect a lower mortality among patients treated at home. A death-rate in the neighbourhood of 10 per cent. is

suggested by general practitioners of wide experience. The mortality from lobar pneumonia among the troops at Aldershot during the 1914–18 War was shown by Abrahams [2] to be as low as 10·5 per cent. Here the patients were mostly picked men of military age, and it is probable that they were moved to hospital in the earliest stage of the disease. At a base hospital in France Malloch and Rhea [3] found a general mortality of 26·1 per cent., with a higher rate among those coming long distances by convoy or hospital train than among base details. Cecil [4], in the United States, reports that the death-rate of pneumococcal pneumonia varies considerably with the class of patient studied, being lowest in private practice, somewhat higher in the hospitals of the better class, and highest in the large hospitals draining the slum areas. Thus the mortality at the Rockefeller Hospital is 19·5 per cent. and at the Bellevue Hospital 35·8 per cent. Among 422 cases (all types) untreated with serum Cecil found a mortality of nearly 36 per cent. Among 429 cases (all types) treated with serum there was a mortality of 28 per cent. Even this lower figure approaches twice the Guy's Hospital figure. It is clear that pneumonia is a more serious menace in the United States than in the British Isles.

Turning to morbidity in hospital cases Waterfield finds that approximately 90 per cent. of the cases which recover do so without disability, so that there is no overwhelming argument in favour of an additional therapy on this score, even though it be shown that serum is capable of producing an earlier defervescence.

Leaving statistical data, let us next consider the factors which are commonly accepted as influencing prognosis in the individual. So far we have recognized that youth and good environment are favourable and that poor conditions and advancing years are unfavourable. Other prognostic indications have been repeatedly observed at the bed-side. The presence of a chronic disease or of alcoholism weights the scales against recovery. Cyanosis is adverse, delirium by no means necessarily so. Wide extent of lung involvement, although frequently, is not always of bad import.

A low and particularly a falling blood-pressure gives cause for concern. The pulse-temperature-respiration ratio affords valuable guidance; while parallelism is maintained or pulse- and respiration-rate are slow in proportion to the temperature hopes are good, but if pulse- and respiration-rate rise unduly while the temperature swings or falls, there is cause for grave anxiety. A clean tongue and nourishment well taken are encouraging. A good leucocytic response, in the neighbourhood of 20,000 cells per c.mm., has always been accounted favourable, and a complete absence of leucocytosis as very unfavourable. Intermediate figures must be balanced with the clinical findings. The pneumococcus may be grown from the blood-stream in the early stages of pneumonia in a certain proportion of cases. A profuse growth or persisting positive blood cultures as the disease advances are now known to be very adverse. Pericarditis and meningitis, other expressions of the septicaemic state, usually foretell a fatal termination. Pneumococcal peritonitis has its special incidence in childhood and may occur with or without evident pneumonia; the death-rate is high but recoveries occur.

It will be generally agreed that prognosis is most difficult during the first three days of the disease—the very stage in which additional help, if required, should be given. Nothing would give a greater impetus to the employment of serum therapy than the establishment of prognostic criteria which would separate at an early stage the 15 or 20 per cent. of cases with an otherwise hopeless prognosis from the 80 or 85 per cent. destined to recover spontaneously. At present reliance must be placed upon clinical judgement of the patient's constitution and reserves and of the extent of the infection combined with a routine leucocyte count, but we *must acknowledge that appearances can be deceptive.* We have all seen the 'apparently hopeless' case recover, and the 'apparently favourable' case succumb.

The Essentials of Non-specific Therapy

Although it cannot be quantitatively expressed it is not to be doubted that symptomatic treatment helps recovery,

and that good or bad treatment may make the difference between life and death. A warm but fresh and well-ventilated room and a good nurse are probably to be accounted of greater value to the patient than all other measures combined. The nurse's mission is to secure the maximum of rest and sleep with the minimum of interference; to supply adequate light nourishment; to attend to the mouth and skin without unnecessary movement or fatigue; to limit the visits of relatives; accurately to keep those records which are of such importance to the physician as indices of progress or deterioration; to preserve optimism; and to administer oxygen and certain drugs at appropriate times. A fussy nurse, too insistent on professional detail or appearances, or too partial to heated rooms and the pneumonia jacket, can do as much harm as her wiser colleague can do good. While most patients are happier propped high with extra pillows, individual requirements vary and the elevation can be overdone. Occasional tepid sponging is n part of the routine. A fluid or semi-fluid diet with fruit-juices and plentiful drinks and additional sugar or glucose is usually the best. Stimulants can frequently be dispensed with altogether if adequate fluid and sugar are taken, or alternatively may be reserved for the anxious days before the crisis. Hypodermic stimulants such as strychnine and adrenaline are, to my mind, of dubious value. They are often given rather at the dictation of anxiety than of necessity, and if they produce a physiological response on the part of the heart or blood-pressure is it not rather by dint of 'flogging the tired horse' and too transitory in its effect to be a real boon? Digitalis is commonly given although it is still doubtful whether it has any virtue in the case of a regular tachycardia and embarrassed function due to fever and toxaemia. Brandy is a food as well as a stimulant and its utility in certain cases and stages is generally approved. Oxygen, preferably given continuously through a nasal catheter, is obviously justified in the presence of cyanosis. For sleep, when pain is slight or absent, Dover's powder with aspirin may be enough for some patients and in small doses is a useful combination in

the case of children. Morphine should never be withheld during the earlier stages in the adult case where sleeplessness and pain are prominent complaints. One quarter of a grain should be the dose, a sixth being too frequently disappointing in its effect. A light flannel jacket or shawl over nightdress or pyjamas is sufficient covering. Heavy poultices, thick or tightly fitting vests, and pneumonia jackets are to be avoided, but a light linseed or antiphlogistin poultice is grateful in the presence of pleuritic pain. So far as is consistent with careful observation the patient should be spared repeated examinations of the chest.

The Method and Results of Serum Therapy

These have been ably summarized by Cecil [4]. The method is based upon successful protective experiments with artificially infected monkeys. Felton's serum has the double advantage over previous preparations of being concentrated, so that smaller quantities can be given at a time, and of being less toxic. The procedure, quoting Cecil verbatim, is as follows:

'The patient is first questioned as to previous injections of horse serum, and as to history of hay-fever, asthma, or hives. An intradermal and a conjunctival test are then made with a 1 in 10 dilution of normal horse serum. If after 15 minutes these tests are both negative, 5 c.cm. of Felton's serum are slowly injected intravenously. If the patient shows no reaction to this first injection of serum, a second of 15 to 20 c.cm. is given intravenously from one to two hours later, and this dose is repeated every two to three hours until the patient has received approximately 100,000 units (equivalent usually to about 100 c.cm. serum). The amount of serum administered on the following day is determined by the clinical condition of the patient. If his condition has improved and if his chart shows a decided drop in temperature, pulse-rate, and respiration-rate, the amount of serum administered is approximately one-half of that administered on the first day. If, on the other hand, the patient's condition is worse, or if it remains unchanged, the intensive treatment is continued. On the third day the same policy is pursued. If the patient's temperature is under 100° F., and if his condition is good, the general rule is to give one or possibly two 10 c.cm. injections to prevent relapse. We have found from experience that if any benefit is to result from serum treatment it is usually apparent after two or at least three days of treatment.'

The difficulties and anxiety attending such a programme outside hospital require no emphasis. Even spacing out the injections to eight hours and giving larger quantities does not greatly simplify, and serum reactions, which are a genuine cause of apprehension, have not been wholly eliminated.

Treating alternate cases without preliminary typing, Cecil obtained a reduction of mortality from 36 per cent. to 28 per cent. in groups of cases numbering respectively 422 and 429. A reduction in the same ratio (provided all cases were seen early enough and considered suitable for serum) would convert the 16 per cent. Guy's Hospital mortality to 12 per cent., and the private practice 10 per cent., say, to 8 per cent.

Approximately two-thirds of all cases of lobar pneumonia are due to Types I and II, and approximately one-third are due to Type I infections. The mortality in Type I cases has been reduced from 31·2 to 20·1 (Cecil) and from 30·0 to 16·6 per cent. (combined results of various investigators quoted by Cecil). In Type II—the most virulent type—the results are less good, a reduction from 45·8 to 40·5 per cent. only being reported (Cecil), and from 37·7 to 24·6 per cent. (other investigators quoted by Cecil). The earlier treatment is instituted the better are the results. Cecil reports a reduction in mortality from 26·8 to 11·7 per cent. in Type I cases treated within 72 hours of onset. I have seen no figures thus far which suggest that the incidence of complications such as empyema is influenced by serum therapy. Armstrong and Johnson [5] also state that complications and sequelae are apparently uninfluenced by serum. The results obtained by the Scottish [6] and English [5] investigators, although their studies so far have been on a smaller scale, support the contentions of Cecil. All observers are agreed that there is an appreciable reduction in mortality and that early defervescence is more frequent among cases treated with serum. Similar claims, it is true, have previously been made on behalf of vaccine treatment and certain forms of drug therapy, but no such carefully controlled studies have been reported by their advocates.

An unexpectedly early defervescence may also occur without specific therapy, but not with the frequency observed in serum-treated cases. Finally, there is evidence for the specificity of Felton's serum in that the mortality of Type III and Type IV infections is not appreciably influenced by it. In other words, improvement depends upon something more than a 'protein-shock' effect. Criticisms of the methods of control employed in the reported series could easily be advanced, for adequate controls in large-scale human experiments of this kind are difficult to come by. Thus in the 'alternate-case' method it is clear that an accidental preponderance of cases of more favourable age and constitution in the treated group would lower the mortality appreciably. However, the factors influencing the liability to death or recovery in pneumonia are so numerous that precise analysis is impossible, and when various groups of reliable workers find essential agreement their opinions must be held worthy of acceptance.

Practical Difficulties of Serum Treatment

(1) These are firstly encountered in connexion with diagnosis, and particularly with diagnosis at a suitably early date. The doctor is not always called at the onset of the disease and two or three days must frequently elapse before he appears on the scene or before the diagnosis is certain. Typing requires a further twelve to twenty-four hours, even if a competent laboratory service be close at hand. Not all lobar pneumonias are pneumococcal and, although an abrupt onset, high fever, and rusty sputum are generally accurate tale-bearers, there are cases in which the differentiation of a pneumococcal from an 'influenzal' or streptococcal pneumonia or a 'mixed' broncho-pneumonia is none too easy. In recent years other types of pneumonia have been more common and pneumococcal pneumonia less common than formerly. Massive collapse in association with bronchitis, a comparatively benign condition, may also be mistaken for pneumonia.

(2) Even allowing that an early diagnosis is achieved

and the case thought suitable for serum, the necessary preliminaries and the frequent administrations of serum by the intravenous route must needs provide the busy practitioner with very real embarrassment. They may also be disturbing, both physically and mentally, to patients for whom we normally advocate the minimum of disturbance.

(3) In the case of a poor patient it must be decided whether to rely upon conservative treatment at home or to risk removal to a hospital where serum treatment can be instituted if the infection prove to be of appropriate type.

While grateful for new knowledge we must confess that it can greatly complicate judgement and practice. We would none of us willingly withhold a curative agent in an anxious disease, but while we know that there is, broadly speaking, a 4 to 1 prospect of spontaneous recovery and a 1 in 3 chance that the infection is of inappropriate type, we may feel a pardonable disinclination to burden a patient with repeated doses of an intravenous remedy for an indeterminate advantage. On the other hand, we cannot put it from our minds that a certain small percentage of otherwise doomed cases may have the balance tipped in their favour by serum.

As an example of the judicial difficulties which may be encountered let me quote the case of a friend and colleague to whom I was called the day after hearing the arguments in favour of serum therapy set forth by its chief exponents.

The patient's age was 63; his life had been healthy and hard-working. On 23 July he felt chilly and unwell. The next day he remained at work still feeling unfit. On the 25th he felt well again. On the 26th he had a rigor while out in his car, and that night his temperature was 102°. I saw him on the evening of the 28th—i.e. the second day from the rigor and the fifth from his first symptoms of infection—and found signs of pneumonia at the right apex and at the right root behind. Respirations 30. Pulse 108. General condition good. Leucocyte count 25,000 cells per c.mm. A small specimen of rusty sputum was obtained. An attempt to type the pneumococcus by Armstrong's [7] direct method was unsuccessful, but the next morning it was reported as Type I.

On 29 July there was considerable restlessness with delirium, and enough cyanosis to justify continuous oxygen at night. On the 30th the left upper and lower lobes became involved. On the 31st he looked

distinctly worse. Respirations 30–6. Pulse 110, with frequent intermissions. Breathing was embarrassed by meteorism, which was relieved by pituitrin and a turpentine enema. There was also severe pleuritic pain below the left nipple. By 2 August (the seventh day after the rigor) the temperature had fallen to 99 6°, the respirations to 24, and the pulse-rate to 92. After steady improvement for a fortnight he began to get up, but then developed a dry pleurisy first at the right and then at the left base without any serious rise in temperature, and with a leucocyte count of only 9,000. The pleurisy took some weeks to clear, but the case gave us no further anxiety.

Here were some of the difficulties. Should I regard the day on which the typing was complete as the third or the sixth day of infection? Accepting it as the third day, should I be influenced by the patient's age and the knowledge that he had a Type I infection and give him serum? Or knowing him to be abstemious and of sound constitution, and comforted by the good leucocytosis, should I rely on the old expectant measures? I chose the latter course, not without heart searchings, but in the event justifiably. In two other cases which ended fatally I have criticized myself afterwards for withholding serum, although at the time I had reasons for my conservatism. From more recent evidence it would appear that the mortality after the age of 50 is little, if at all, influenced by serum.

Conclusions

It remains to attempt advice in practical form. At present no unalterable rules can be laid down with regard to the indications for serum in lobar pneumonia. As in all therapeutic decisions the final plan must be based upon the particular state and requirements of the individual patient. The method is clearly, and (unless it can be simplified) must remain, more suited to hospital than home conditions. It is contra-indicated in children and adolescents for the most part, since the natural recovery-rate is so high in this age-period. It may reasonably be decided to dispense with it in advanced age when interference is ill-tolerated, and the disease frequently provides a blessed escape from infirmities. I should personally hesitate to employ it in any subject with known allergic tendencies, for I am doubtful

whether the ill effects of serum shock at the beginning or of serum sickness at the end of a pneumonia would be proportionately counterbalanced by the benefits of the treatment. In previously healthy adults showing a good initial response to infection and a high leucocytosis, I should feel justified in withholding serum. We are thus left with adult cases giving cause for undue anxiety at an early stage and showing a failure of leucocytosis; alcoholics might be included in this group. To these it should be justifiable to give an early dose of Felton's serum, and to continue the treatment if the organism is found to be of appropriate type. The treatment is more worthy of consideration in Type I than in Type II infections. At present these restrictions would seem to me reasonable in institutions where costs must be carefully counted, and in private practice. Expense prohibits the treatment of poor patients in their homes. In such cases the difficult decision of whether or not to counsel removal to hospital must be made. If the disease has reached its third day and adequate nursing and attention can be secured, I should usually prefer to keep the patient at home and to forgo the possible advantages of laboratory study and serum therapy. Removal, if necessary, should be carried out within the first 48 hours.

While the employment of serum in pneumonia on a wide scale cannot be advocated, its claims cannot be overlooked. It is furthermore possible that a collective investigation of prognosis and a more critical search for special indications may serve to lighten the physician's burden of decision, to simplify his task, and to reduce a little further the comparatively low death-rate from pneumococcus Types I and II which obtains in this country among previously healthy persons. Of our 15–20 per cent. of deaths, be it remembered, a certain proportion occur among 'bad lives' which are unlikely to be reclaimed by any treatment. Others again are due to infective strains against which we have as yet no potent serum. With a suitable card system observers in general practice might, I believe, greatly assist a collective inquiry into the matter of prognosis. It is to be hoped that hospital and laboratory workers will continue their

studies of method and indications, and that the firms responsible for the supply of serum will find it possible to reduce the costs.

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This chapter has been left as it originally stood in illustration of the state of knowledge regarding prognosis in lobar pneumonia and the effects of treatment on it prior to the introduction of the sulphonamides and penicillin. We still require more precise knowledge of the special indications of different age-periods. It is not always kind to reclaim the very elderly with potent remedies which may check their lung disease but fail to give them back their faculties and enjoyment of living. The actual mortality for the several age-groups and the different socio-economic groups and in types of pneumonia not due to the pneumococcus have also to be better determined for countries, races, and communities and in separate epidemic periods. Without them therapeutic assessments will remain incomplete and less reliable than they might be.

XX

PROGNOSIS

THE three main tasks of the clinician, be he physician, surgeon, or specialist, are diagnosis, prognosis, and treatment. Of these diagnosis is by far the most important, for upon it the success of the other two depends. It is, however, with prognosis as a part and product of clinical discipline that this chapter is concerned. In my recollection it has been a common grumble among students that ward teaching, as a whole, is over-insistent on diagnosis and allows too little time for therapeutic discussion. I remember no such reference to the neglect of prognosis in bedside teaching. At that stage, perhaps, the student has scarcely come to a full recognition of its importance. And yet, difficult though it be, instruction in prognosis should surely be given far more consideration than it commonly receives. It should anticipate treatment in the discussion at the bedside—or, preferably, at a discreet distance from it. Diagnosis is really incomplete and sound treatment and the assessment of the results of treatment are *impossible without that rational* forecasting based on pathology, statistics, and observational experience which we call prognosis. Prognosis requires a better appreciation of the whole pathology of a case or a disease than present diagnosis, and although the future contains even more variables and unknowns than the recent past, it is none the less possible to establish guiding principles in prognosis which improve method and bring advantage to the patient and his doctor and, in many conditions, allow a high degree of accuracy. Prognosis is essentially a physicianly task. The pathologist, the biochemist, and the radiologist, although they may greatly assist that task, have no immediate concern with it. The study of prognosis is sometimes considered academic rather than practical, but this is a narrow and unwarranted view. For the sake of our patients and their relatives and for the ordering of our judgements it is a daily duty; for the improvement of our under-

standing of pathological processes and to help us to see them in their true perspective it is an essential discipline.

The Meaning and Uses of Prognosis

Hippocrates said: 'I hold that it is an excellent thing for the physician to practise forecasting. For if he discover and declare unaided by the side of his patients the present, the past and the future, and fill in the gaps in the account given by the sick, he will be the more believed to understand the cases, so that men will confidently entrust themselves to him for treatment. Furthermore, he will carry out the treatment best if he know beforehand from the present symptoms what will take place later.'

These views and the famous prognostic aphorisms were based on clinical experience alone, with none of the checks or confirmations furnished by pathology or by biochemical or other modern assessments of degrees of tissue damage or functional impairment. In this regard they may appear the more remarkable, but we should also remember that, lacking scientific aids and specific remedies, Hippocrates was, in fact, compelled to train his mind and form his judgements on the basis of an undistracted study of the natural course and history of the diseases which came to his notice. In other words, he employed methods appropriate to what would now be called the Follow-up Clinic, of which he may, perhaps, be acclaimed the first founder.

An understanding of the natural or undisturbed course of a disease must provide the basis of all prognostic assessments. In many conditions to-day this course can be greatly modified by specific treatments, by surgery, or by altered modes of life. In other conditions our endeavours still have little influence. In others again unwise interference may, and too often does, give an adverse bias to the patient's prospects. Advancing knowledge has both assisted and complicated prognosis. The assistance has come through new diagnostic methods and tests of function and the provision of specific remedies; the complication through the influence of new and potent, but sometimes more hazardous treatments, or the multiplication of alternative treatments. To take an

example, we now have more precise methods of assessing degrees of thyrotoxicosis. By means of improved assessments we have to decide between medical treatment, X-ray treatment, and operation in the individual case. Either the withholding or the employment of a particular measure may entail risks to health or sometimes even to life.

Prognosis is often held to imply no more than a decision as to whether the patient will recover or not, or an estimate of the duration of his disease. Just as diagnosis means 'through' (or thorough) knowledge of a case and is something more than mere nomenclature or a label, so, too, prognosis (or foreknowledge) should mean a visualization nnd reasoned presentation of all the events which are likely to mark the future course of a particular disease nffecting a particular patient, and not a mere forecast of duration and outcome. Nevertheless, judgement in practice must clearly be guided by mortality statistics and a knowledge of the prognosis of diseases as a whole, be they dangerous or trivial.

Prognosis as a Duty

In what respects is prognosis to be regarded as a duty, that is to say as a normal and proper physicianly function? In all serious illnesses, in many less serious conditions, and in some which are trivial in the doctor's eyes, but nevertheless a cause of anxiety to the patient, the main interest of the patient and his relatives (apart from the immediate relief of symptoms) is to know what the issue of the illness will be rather than its precise nomenclature. They do, in point of fact, want to know the diagnosis, but solely or chiefly as a guide to prognosis. A troublesome cough or an abdominal pain is apt to imply pulmonary tuberculosis or appendicitis or cancer to the lay mind until assurance is given to the contrary. Comfort and reassurance, indeed, play a part in treatment which, although their influence cannot be measured, are universally accepted as essential contributions to progress and even to recovery. In organic as well as functional diseases we are becoming steadily more impressed by the inter-relationships of emotion and bodily change. Anxiety is the most prevalent of all the harmful

emotions. *The best counter to anxiety is a good prognosis.* It is not without significance that the ablest and most successful physicians have also included among their number the most optimistic. A change in the whole feeling and attitude of a patient and his or her relatives not infrequently dates from the visit of a family doctor or consultant who has been at pains to emphasize the likelihood of a good recovery. I find it difficult to credit that there exist doctors who tell their patients—save in exceptional circumstances—that their condition is hopeless, and yet in taking histories how often one has been told that 'my doctor said I could not recover', or 'they only gave me a week to live', or 'three doctors gave me up'. Let us admit that patients, like all of us, are apt to exaggerate dramatic or adventurous experience, and that usually these gloomy prognostications must have reached them at a later date; even so it is clear that the relatives must have had to submit to an unnecessarily sad and head-shaking interview. Such pessimism, and this is the point I would make, is repeatedly proved unjustifiable by the event. Doctors, in other words (although their good prognoses are more rarely wrong), repeatedly fall short in their prognostic judgements. Need they fail so often and need their bias so frequently be adverse? Excepting in inoperable cancer, until lately bacterial endocarditis, a few other rare progressive maladies, and obviously moribund states, we have no such certainty of a fatal result as some of us are apt to assume. The longer we live the more lessons we receive in respect of the remarkable recoverability of the human body from grave diseases, from pneumonias and septicaemias, from heart-failures and grave haemorrhages and accidents. Very few of the common acute diseases have an over-all mortality even approximating to 50 per cent. *Excepting at the extremes of life and in a small group of* diseases at present unconquerable the chances of recovery are generally greater than those of demise. Children especially have great recuperative powers.

It is therefore wise and just to make a point of giving a good prognosis (whether the patient has questioned it or not) in all cases in which the clinical evidence and pathological

knowledge allow it, and where doubt exists at least to give the patient the benefit of the doubt. In cases where the doctor himself is nnxious and uncertain it is still reasonable nnd kindly and useful to stress the favourable points in discussing the case with relatives and, as for the patient, to congrntulate him on his gains, his courage, and his co-operation while excluding adverse auguries from the conversation. In the process of assembling 'pros' and 'cons' for the communicated opinion, the considered prognosis takes better shape; the partial expressed opinion, in fact, assists the whole reserved opinion. Sir Alfred Fripp used to say to bis students, 'If we cannot be clever we can always be kind'. With experience and the years to help us, we need not despair of educating both qualities. In states of ill health due to anxiety, and especially in those due wholly or partly to the fear of disease, a good prognosis is almost the whole of treatment and frequently achieves a cure.

Just ns a good prognosis is calculated to do good, so, too, a bad one may do nn infinity of harm and cast a cloud of gloom upon a household which will with difficulty be prevented from finding its way into the sick-room. Some men through native caution or a fear of loss of reputation decline to say openly that a patient may get well when it seems possible that he may die. To give no prognosis is almost as culpable as to give a bad one nnd is an evasion of responsibility. It is always possible to give what is called a 'guarded prognosis'. Wrongly placed optimism, provided it is not careless or breezy or accompanied by a disregard for sensibilities or a neglect of therapeutic detail, will rarely be beld against a doctor. Wrongly placed pessimism, on the other hand, will always be held against him and even pessimism justified by events quite frequently so.

You may say that this policy of the reassuring prognosis is not compatible with intellectual honesty. I believe it to be perfectly compatible, so long as we do not delude ourselves. As scientists we do not bow to the foolish and impossible request of the law to tell the whole truth and nothing but the truth. We discover as much of it as we can, but remembering the limits of our precision we should recognize that

it would be as unjust, through fear of error, to withhold comment on the more favourable features of a case, however few they be, as it would be to withhold any other helpful measure of treatment. If or when the outlook becomes absolutely bad, then we must impart our view to the relatives. Before that it is no failure of duty or honesty of purpose—while the mind is taking counsel with itself—to give rather more hope than the moment's uncertainty may seem to justify.

It is very important at times for the patient or relative to know how long an illness will last. If the illness be pneumonia or a duodenal ulcer or a Pott's fracture we can give a fairly close estimate both in regard to the bedridden and the convalescent phases of treatment. In other conditions we may only be able to give a very rough estimate, but for economic and other reasons even this is greatly appreciated.

Prognosis is a duty in another important sense in that it must constantly guide our treatment. To this end we must formulate our judgements with the greatest accuracy possible, assessing the probable course of the disease, learning (in order to foresee) complications which may demand alterations in treatment; visualizing, in short, a total or consecutive rather than an immediate pathology. We should also train ourselves to observe the strictest impartiality in assessing the proportionate contributions of time and nature on the one hand and of our own ministrations on the other. To accomplish all this we must needs be as diligent in our search for *prognostic* as for *diagnostic* signs.

Before leaving this aspect of the subject let me relate a single case in which the outlook seemed desperately bad, but in which a grave prognosis proved to be quite unjustified. Any physician or surgeon of experience will have seen other cases in plenty which seemed as desperate but in which recovery followed.

Case 1. Many years ago I was called in consultation to the case of a young woman in the sixth month of pregnancy who had fallen victim to a very severe attack of anterior poliomyelitis, sustaining a flaccid paralysis of all four limbs and many trunk muscles. As there was no early improvement and as the possibility of her going through the later

weeks of pregnancy and parturition seemed out of the question, an attempt was made to induce labour. This failed, and a Caesarean section was performed. A few days later she developed acute intestinal obstruction from an adhesion between the small bowel and the uterine scar. With extensive paralysis in numerous muscle groups, profound exhaustion, persistent tachycardia, and some respiratory embarrassment, her condition seemed desperate and her hopes of happy and active life remote even should she survive another operation. Several colleagues met in consultation. At first I argued that it might be kinder to give morphine and interfere no more. An older and a wiser physician took the view that we should still seek to save life and that we could not forecast the degree of recoverability of her paralysed muscles. A Paul's tube was inserted and she recovered from the emergency. But she did more, for gradually, after months of weary waiting and devoted care, she made an almost complete recovery from all her disabilities and was able to walk and dance and lead a happy, active life again.

I have never been a pessimist. From this case I learned two valuable lessons: (1) that there were even fewer occasions than I had supposed for absolute pessimism, and (2) that the most extensive cases of poliomyelitis sometimes make the most complete recoveries. Had the case been one of intestinal obstruction from an inoperable and painful growth in an old, enfeebled person, the judgement might obviously have been a very different one, for the ultimate issue and the intervening misery, despite a temporary relief of the obstruction, would have been disputed by none.

Prognosis as a Discipline

There is always a pleasant sense of satisfaction in the achievement of a correct diagnosis. It is just a little too easy to rest on the laurels of that achievement. As I have elsewhere insisted, diagnosis should strictly mean the thorough knowledge of a case. It involves not merely a correct label, but an understanding of the patient, a familiarity with his environment and with the antecedents of his malady, an appreciation of his inherited constitution and his psychological type, together with a proper appraisement of symptoms, signs, and accessory findings. It requires a working knowledge of morbid anatomy, physiology, and psychology. Prognosis requires all these and more. It requires acquain-

tance with mortality and morbidity statistics, with the death rate in different age periods, with the constitutional factors which increase or lessen morbidity, with the good and bad effects in differing circumstances of certain treatments, with the signs and symptoms not merely of the disease but of a good or bad response to the disease. Prognostic ability, in brief, is born largely of pathology and patiently gathered clinical experience. It evolves even more slowly than diagnostic ability. Minute and careful clinical observation, a good visual memory, and that necessary inquisitiveness about the subsequent course of cases which is nowadays systematized in the follow-up inquiry may all be numbered among the handmaidens of prognosis.

Prognosis might almost be defined as the continuous study of living pathology and in this, although it is often accounted an art, I would submit that it can become a scientific process. We are sometimes too content with a static pathology, but a biological process, whether physiological or pathological, is never static. Inflammation spreads or recedes, bleeding is arrested or continues, destruction and degeneration advance or are succeeded by repair. Whether through clinical, pathological, statistical, or other methods, we should bend our best endeavours to making prognosis more scientific. Science is not only that which is deemed exact. The science of meteorology is partly concerned with prognosis and bases its forecasting on scientific observations. Like medicine, its prognoses are baffled by unknowns and variables. Whether they will ever attain such a degree of accuracy as medical prognosis, for all its shortcomings, has already attained I cannot say. Weather forecasts can concern themselves with short-term judgements only. Medicine has a constant interest and a considerable tale of achievement both in immediate and remote prognosis.

Strictly speaking, the physician should ask himself in every case: (1) What is the immediate prognosis? (2) What is the remote prognosis? (3) What are the possible complications by the way? (4) How may age or other circumstances peculiar to the patient influence the course of his disease? (5) How will this or that treatment alter the outlook?

In lobar pneumonia age, physical type, personal habits, previous health, extent of lung involvement, the pulse-temperature-respiration ratio, the presence or absence of cyanosis, the leucocyte count, the type of pneumococcus all have a bearing on prognosis. Specific chemotherapy and penicillin have introduced another favourable factor. As a useful background we know that in the majority of cases the disease will have terminated within ten days and that in this country the general recovery rate before the arrival of the new remedies was about 80 per cent., with a favourable variation in childhood and adolescence and an adverse variation towards and after middle life.

Hour-to-hour observation in one disease, day-to-day or week-to-week observation in another, may modify opinion. The information necessary for accurate assessments is often available if carefully sought for. In ninety-nine cases a boil on the neck gives us no great anxiety, but we must never forget that through natural accident or ill-judged treatment the hundredth may give rise to a metastatic renal abscess or a fatal septicaemia. A cancer of the stomach may be operable or inoperable. Depending upon its position and rate of growth it may run a variety of courses, with or without pain, with or without obstruction, with or without severe anaemia. We need to know and should try to forecast the likely course in each case, however hopeless the ultimate issue may be.

Books and teachers can tell us a great deal, but our own senses and the experience of the years tell us a great deal more. Prognostic ability of high grade can only come with long experience, but, clearly too, the earlier we begin to practise prognosis in a systematic manner the better it will be for our minds, for our patients, and for the trust which they impose in us. This practice is a part of what I frequently refer to as 'clinical discipline', and the best discipline, when teaching has provided the rudiments, is self-discipline. We must set ourselves standards in observing, in note-taking, and in critical commentary. We must always prefer facts to opinions. If we say or hear a teacher say, 'I believe this patient will get well', we must proceed to discover and

analyse the reasons upon which that opinion was based, and, if it proves correct, to review the significance of the signs which instructed the belief. In subsequent cases of the same kind we are then able to test our experience and by degrees to appreciate which clinical phenomena have acquired a positive or negative value.

The Influence of Prognosis on the Assessment of Treatments

I have hinted already that we have no right to conclude that a particular treatment is effective in a particular disease unless we have first familiarized ourselves with its natural prognosis or its prognosis under conditions of purely symptomatic treatment. Neglect of this simple principle has been responsible for countless misjudgements and a great waste of time and money, and has caused inconvenience, discomfort, and even death to a large number of patients. I have dealt with this subject elsewhere,[1] but must make a further brief reference to it here. Gull showed us long ago how to avoid large errors in therapeutic judgement when, in answer to some of his contemporaries who claimed that they had specific remedies for rheumatic fever, he devised the simple experiment of treating a series of cases with mint-water. He was thus able to show that the mortality and morbidity were no worse and the duration of fever no longer in his cases than in theirs and that their claims were thus unsubstantiated. In brief, he studied the natural prognosis of the disease and thereby corrected fallacies. Vaccines, sera, operations, and proprietary remedies galore have been employed and are still employed in the same indiscriminate way as Gull's contemporaries employed their cures for rheumatic fever and with as complete a disregard for the lessons of natural prognosis. Only when a treatment has a physiological basis proved by animal and human experiment (as in the case of insulin and liver-therapy) or when, with its physiological or pharmacological basis still to be proved (as in the case of sulphonamides, penicillin, and quinine)

[1] 'Prognosis and Therapeutic Principles' (*Brit. Med. Journ.*, 1936, ii. 1067).

large-scale comparisons are possible between the natural and the modified prognosis, are real advances in therapeutics made. A few years ago an injection reputed to assist the cure of peptic ulcers was launched with rosy claims but with quite inadequate experimental proofs and with no preliminary clinical trials. For a year or more it had a great vogue. Now it is never heard of. Those physicians who at first advocated it, claiming that at least it relieved symptoms quickly, overlooked entirely the elementary fact that ulcer *symptoms undergo spontaneous remission with great frequency* and in duodenal ulcers almost with regularity. They did not know the natural prognosis of the disease. Surgeons and endocrinologists have discussed the merits of operation and hormone therapy in the treatment of undescended testicle. Some years ago I had the pleasure of reading a thesis written by a school medical officer, Dr. L. S. Marshall, of Taunton, who showed that in a series of 1,910 schoolboys, ranging in age from 5 to 16 years, undescended testicle was observed in 5·1 per cent. Of these just over a half showed bilateral non-descent. Spontaneous descent occurred before puberty in 95·7 per cent. of cases. Without basic knowledge of this kind no sound conclusions could be drawn in regard either to the new or the older method of treatment. Therapeutic enthusiasm and bias are dangerous. The study of natural prognosis is a corrective to both.

The Influence of Diagnosis on Prognosis

It might seem absurd to discuss the effect of diagnosis on prognosis. Clearly an accurate prognosis cannot be made if the diagnosis on which it is based is wrong. A diagnosis may, however, be correct in name but only partially correct. A patient may consult you with angina pectoris. If the symptoms be due to an underlying anaemia or anxiety or have a slight physical basis with a large nervous aggravation and you give him the prognosis due to a case with advancing coronary disease, you will not only give a wrong prognosis but you will also do your patient harm (1) through denying him the correct treatment and (2) through increasing an existing anxiety. Angina pectoris, in fact, is not a diagnosis

but a symptom. A familiar nomenclature used as a diagnosis commonly influences prognosis and treatment adversely. Here are cases in illustration of these points:

CASE 2. A man in the middle fifties had been troubled for two and a half years with effort angina. Prior to its development he had passed through a period of very considerable anxiety and had lost a near relative from heart failure. He had restricted his activities to an extreme degree, having previously led a very active life. He and his wife were both unhappy and anxious. No contra-indications to a good prognosis and increased activity were found on the physical side. Psychologically a good prognosis seemed to be the wisest prescription. From that moment improvement was steady, and four years later he was reported to be in good health and busily employed in many useful ways.

CASE 3. I was consulted by two very anxious parents on behalf of their small boy, aged 7, who had frequently recurring seizures with transient loss of consciousness. I had no doubt that they were allied to epilepsy, but they were different both in their description and in their great frequency (up to 18 fits a day) from ordinary epileptic attacks. On this account I took a reassuring line and redoubled the reassurance when I learned from Sir Charles Symonds that the description I was able to give him was that of pyknolepsy, a variety of seizure which I had not previously encountered and from which recovery is usually complete by puberty. Ten years later I received a grateful letter from the mother to say that the prognosis had been fully justified and that the boy had been completely strong and well and had entirely outgrown the attacks from the age of 13.

Once more an epileptiform attack is only a symptom or syndrome and, like angina pectoris, may carry very different prognoses. These in their turn must influence the lives and happiness of patients for better or for worse.

THE INFLUENCE OF TREATMENT ON PROGNOSIS

The influence of specific treatments on prognosis can be assessed with considerable accuracy, provided we recognize the effects of such variables as age, the duration of the illness, and the expert knowledge of those in charge of the treatment.

It is almost impossible to measure the influence of symptomatic treatment on prognosis. Can a timely hypnotic or stimulant save life? Can a gentle and a skilful nurse or a cheerful sensible doctor make a difference between life and death, as compared with a dour and clumsy nurse, or a dull

and careless doctor? Such questions we cannot answer with proofs, but we find it hard to doubt that the summary of symptomatic ministrations frequently determines or hastens recovery. Well-timed and well-chosen surgical treatment or specific therapy can undoubtedly and in numerous circumstances save lives that would otherwise be lost, but withholding surgery and specific treatment in certain circumstances may also improve prospects.

The real personal difficulties arise in those cases in which the arguments for or against operation or a drastic measure of treatment are evenly balanced. Then the simplest and most direct question we can put to ourselves is this: 'Are the risks of this operation or treatment, on the evidence before me, less or greater than those of the disease left to Nature and symptomatic methods?' Operation is the treatment of choice in appendicitis, but there are cases and stages and complications of appendicitis in which prognosis (even though the symptoms are very anxious) is better with delay than with immediate action. A treatment, in fact, should not be employed because it is the official treatment for the disease from which your patient is suffering, but because you believe his particular prognosis will be improved by it.

Again, in anxious situations it is reasonable to pause and ask oneself: 'Would I wish this method to be employed if my own wife, mother, or child were the patient?' In asking this question we help to balance belief in a method or its advocates against personal responsibility subjected to its sternest test, thereby weighing prognosis in the most critical scale that conscience can devise.

Temperament, Anxiety, and Prognosis

There can be no doubt that the emotional qualities of the physician may considerably colour his judgements. I had a good friend, now dead, who was an able diagnostician but noted for his gloomy prognostications. Although his reputation was large he must have lost not a little practice in proportion to the loss of hope which he unwittingly engendered in the hearts of patients and their doctors. Men like Sir William Gull, Sir James Goodhart, and Sir William

Osler—all great and wise physicians—were reasoning optimists and their practices were large in proportion to their generous natures and forecasts.

There is not one among us, however, who can escape the influence of anxiety in harassing situations, and anxiety cripples judgement. This is at no time better manifest than when sickness comes to the doctor's family. With rare exceptions, doctors find themselves incapable of sound judgements about their own wives and children, and prefer to summon the help of colleagues. An illness which would cause no alarm in a neighbour's wife can bring to mind all the gravest complications in your own.

There are, however, many other occasions in the course of practice in which anxiety is so great as to hamper decision. Here again self-discipline may lend a helping hand, and by sitting down to the facts of the case in the evening (remote from the appeals of an unhappy household and the threatening outward aspect of the illness itself), by totting up the favourable and unfavourable features, recalling past experience or talking the problem over with a friend or partner, reason is recalled and we are enabled to give a just prognosis, carrying its message of hope in one case or regretful anticipation of further anxious days or weeks in another. Both in diagnostic and prognostic problems I have occasionally resorted to a sheet of paper and set down the 'plus' and 'minus' marks in two columns, not expecting a mathematical decision therefrom, but just as a means of balancing my thoughts.

Prognostic Method

It would require a book rather than a chapter to describe the rules of guidance appropriate to the prognosis of the various types of disease. Let me take just one example before I conclude, one which will frequently be encountered in practice, which has many anxious complications, but which is, on the whole, too gravely regarded by doctors and much too gravely by the laity. It is one which should have a special interest for Guy's men in that its morbid anatomy was first thoroughly investigated by Richard Bright, while

its clinical and pathological aspects were successively studied by Gull, Wilks, and Mahomed after him. Originally included under the heading of Chronic Bright's Disease, it is now more usually referred to as Hypertension, or preferably Hyperpiesia, or simply as High Blood Pressure. Here is a disease with a slow, insidious course, with a liability to death in the long run from cerebral haemorrhage, congestive heart failure, coronary occlusion, or combined cardio-renal failure.

The age, weight, sex, occupation, mentality, mode of life, and family history, the symptoms and physical findings in the individual case may all influence prognosis. The judgements are built upon clinical experience and morbid anatomy. Is it possible to balance the evidence in such a way as to impart a useful degree of accuracy to our opinions?

If the patient is a man aged 50 and his forebears have died suddenly of strokes or heart failure during or before the sixth decade, if he is overweight and lives too well or works too hard his prognosis is likely to be worse than that of a man of the same age with the same blood pressure, but who is lean and lives carefully and has a negative family history, or of a woman of the same age who has developed the high pressure of the menopausal years.

But let us confine ourselves in this instance to objective findings and see if we can usefully place our patient in one or other of four prognostic categories which have seemed to me convenient and useful in these difficult assessments.

In the first category the patient has been discovered to have a high blood-pressure in the course of a life assurance examination or has presented himself with minor symptoms of fatigue or irritability. His systolic pressure on more than one occasion is 170, his diastolic 100 mm. of mercury. His radial arteries are not appreciably hard, his apex beat is within the nipple line, his retinal arteries are barely beginning to dint the veins. His urine is of low specific gravity, but contains no albumen. He has had no warning signals and has developed no appreciable structural changes in heart, arteries, brain or kidneys. His diastolic reading, which helps to tell the state of the arterial wall, has not risen unduly.

There is no need to give a gloomy prognosis. He may live ten years without illness or vascular accident. Weight reduction, if needed, sensible modifications of life and good holidays should nevertheless be counselled.

In the second category the artery is palpably thickened, the systolic pressure is 220 and the diastolic pressure 110 to 120, the apex beat is half an inch outside the nipple line, there is a solitary retinal haemorrhage and the urine contains a trace of albumen. Minor secondary changes have, in other words, began to appear. There are still no major warnings of catastrophe, but it has become likely that a more serious damage to brain or heart will follow in the next two to five years. Careful modifications of habit may still diminish risks and postpone the evil day, but the prognosis must now be more guarded.

In the third category a vascular accident affecting an important organ, a coronary or cerebral thrombosis or a cerebral haemorrhage, has occurred, or the earliest symptoms of congestive failure have announced themselves. Perhaps Cheyne-Stokes breathing is noticed on the consulting-room couch or there have been attacks of nocturnal dyspnoea in threat of left ventricular defeat. The diastolic pressure has risen to 140 or 150. There are several haemorrhages and white patches in the fundi. There is a heavy cloud of albumen. Periods of rest in bed have become necessary. Improvements are temporary and incomplete. Death within a year has become probable.

In the fourth category our patient is bedridden with heart failure and oedema or the progressive mental deterioration of cerebral arteriosclerosis. There has been a fall in the systolic pressure, but the diastolic figure remains too high. Days or weeks or, at the most, months is the best forecast we can offer.

At each of these stages advice and treatment must be determined by the prognosis which we construct from a combination of clinical experience with pathological insight. At no stage is the construction of the prognosis merely an academic exercise. But how often is the pathological insight lacking and how many patients are worried into a quite

unnecessary anxiety and ill-health because of this lack. The world is full of unhappy, careful, middle-aged people who would have remained active for many more years had not doctors ascribed to a column of mercury a degree of prognostic reliability which it can never alone possess, and forgotten both their morbid anatomy and the importance of studying 'the whole man'.

Conclusion

I had almost omitted to mention prognosis as an academic exercise, so many practical lessons have I found for it. Let us add now that anything in our work which trains the senses and sharpens the wits, compels discussion, invites analysis, and excites interest, also brings gifts to intellect and personality over and above the general gifts of a professional life. It helps to satisfy a hunger and to nourish clear thought and to foster that spirit of natural philosophy which should find a home in the heart of every physician. I would therefore commend the study of prognosis as a salutary exercise, as an individual adventure in consecutive pathology, and suggest for serious consideration that the follow-up investigation, be it private or institutional, and the wider use of statistical analyses have many far-reaching contributions to make to medical knowledge. In the years ahead they must be regarded as essential activities of all hospitals and clinics.

For the individual student it would be no bad exercise to include a footnote on estimated prognosis at the beginning of every case-report, with a correction when possible at the end.

XXI

THE RADIAL PULSE[1]

From the earliest times the examination of the pulse at the wrist has been a familiar and important medical ritual. It has lost nothing of its importance and remains the most frequent of the scientific observations of daily practice. I say 'scientific' for, in counting the pulse, we are making an accurate numerical record which may be compared with known standards, and the personal equation plays no such part as it does in the assessment of many signs and symptoms. In determining the qualities of the pulse we may make other valuable observations, but our estimates, not being measurable by the unaided finger, lack precision.

In a slender volume by William Heberden, with the comprehensive title—*Commentaries* on *the History and Cure* of *Diseases*—is included a small paper which I often peruse with pleasure. Its subject is 'Remarks on the Pulse', and it was read at the College of Physicians on 7 July 1768. It has not attracted the attention rightly given to his account of angina pectoris, the first and best account ever written of that disorder, but like so many of Heberden's writings it is remarkable for the accuracy of its clinical descriptions, for the soundness of its conclusions, and for the pleasing simplicity of its style. It interests me to think how gratified Heberden would be, if he were to return to-day, to find so many of his opinions unaltered by the passage of time. How eagerly, too, he would accept and welcome the newer and more certain knowledge which has been won through the agency of instrumental device.

It is well for us to take stock occasionally of what has been added to our store by the introduction of methods and instruments of precision. Physicians, even if they handle none of these but the sphygmomanometer, must remain in constant debt to Sir James Mackenzie, Sir Thomas Lewis, and others, for the light which their researches have thrown upon many familiar and other less familiar pulse pheno-

[1] *Guy's Hosp. Gazette*, 1930, xliv. 26.

mena. It would, I believe, be perfectly fair to claim that we can now, as a rule, get on very well in practice without the sphygmograph, the polygraph, or the electrocardiograph, but our ability to do so is in great part due to what we have learned from them, and in certain situations we shall continue to require their aid if we are to give of our best in diagnosis, prognosis, and treatment.

My present plan, however, is not to inquire into this indebtedness or to discuss the physiology of the radial pulse, but rather to consider what diagnostic information can be obtained by us, employing only, after the manner of Heberden, the unaided finger and the radial arteries of our patients. By 'diagnostic information' I mean such as will, without further ado, allow a positive diagnosis or strongly support or suggest a diagnosis. I need hardly add that we should never rest content with this evidence alone, and that my purpose is rather to indicate how helpful so simple a proeedure as feeling the pulse may sometimes be than to encourage undue reliance upon it.

There are five particular observations which may be made on the pulse, some of which we make eonsciously or half-consciously every time we put a finger to a wrist, but all of which in certain types of case we should be at pains to make and to record. I refer to (1) the rate, (2) the rhythm, (3) the volume, (4) the tension of the pulse, and (5) the state of the artery.

For convenience, however, I shall here consider abnormalities of pulse behaviour under three headings, namely, *altered rate*, *altered rhythm*, and *altered quality*—allowing quality to speak for volume, tension, and the state of the vessel. You will appreciate that rate, rhythm, and quality may be severally or simultaneously modified. You will also observe that pulses may be diagnostic of general as well as of cardiovascular diseases.

Altered Rate

Heberden, wisely partial to matters of fact, devotes a large part of his paper to pulse-rate or frequency. We all know that the rate of the pulse in health varies with age,

year or two ago with basal congestion and slight haemoptysis in which my house physician feared pneumonic tubercle, but the history and the pulse peculiarity, with a rate of 150, in a patient seeming singularly little perturbed, suggested some form of paroxysmal tachycardia, and this was proved by an electrocardiogram to be due to 'flutter'. Very high rates and sometimes paroxysmal behaviour also occur with *auricular fibrillation*. With the high rates it is often difficult to appreciate the presence of arrhythmia. A woman, aged 54, had a pulse-rate in my consulting-room of 160 to the minute and over, and (as I noted it at the time) the pulse was, so far as the finger could determine, 'practically regular'. But her bouts, as she described them, did not end abruptly, the tachycardia had now become persistent, and her appearance suggested organic heart-disease. An electrocardiogram showed auricular fibrillation, and she responded very well to digitalis. When, therefore, the clinical features do not accord with a simple paroxysmal tachycardia we must have the assistance of an electrocardiogram, for without it appropriate and valuable treatment cannot be happily instituted and controlled.

Bradycardia, with pulse-rates in the neighbourhood of or just below 50, occurs in some big, robust men in health; after certain fevers; with jaundice, starvation, and cerebral compression; and sometimes in myxoedema; but in none of these is the pulse-rate alone diagnostic. A pulse-rate of 30 or less, however, nearly always means complete heart-block, and so enables us to diagnose, with a finger on the wrist, a lesion of the auriculo-ventricular bundle. It may so serve to explain, without further inquiry, fainting attacks or fits which had otherwise remained obscure. To feel the uncomfortable pause between beats in these cases is a strange experience and not easily forgotten.

Altered Rhythm

Other alterations of rhythm may be correctly assessed with a finger on the wrist, but I shall only dwell upon one significant and one less significant type of arrhythmia, both of them common in practice.

that they are not worth regarding in any illness, unless joined with other signs of more moment. They are not uncommon in health, and are often perceived by a peculiar feel at the heart by the persons themselves every time the pulse intermits.'

Actually I suspect that it is the compensatory pause which gives the 'peculiar feel at the heart'. He even pursued to necropsy the case of a woman dying of cancer who had had an intermitting pulse from her youth, and 'an able anatomist' could demonstrate no disease of the heart, pericardium, or great vessels.

In diagnosing extra-systoles, therefore, you are often in the happy position of being able to diagnose something that does not much matter and so can the better reassure your patient.

Altered Quality

There is a remarkable type of pulse associated with the name of Corrigan, a Dublin physician, and alternatively described as the water-hammer pulse, which is characteristic of incompetence of the aortic valve. It is best felt, not with the finger-tips, but with the palmar aspects of the fingers laid across and embracing the flexor aspect of the patient's wrist and with his arm raised above the level of his chest. It can frequently be recognized without this manoeuvre, but with it the peculiar shock-like sensation accompanying the sharp thrust and quick recoil of the artery are better appreciated, and the ulnar pulse—not as a rule easily found—is simultaneously felt. I find that most of my clerks have no idea as to why it is called a 'water-hammer' pulse. A water-hammer is a physical toy and consists of a glass tube half filled with water from which the air has been largely exhausted. When it is tilted the water falls with a peculiar slap to the other end of the tube, so that the name is quite appropriate. Pulses of water-hammer type are also felt in severe anaemias, especially in the recovery phase after recent haemorrhage, and frequently also in elderly folk with rigid thoracic aortas. But in its most developed form the water-hammer pulse proclaims an aortic leak. Aortic incompetence is a result of rheumatic or infective endocarditis or syphilitic aortitis.

Aortic stenosis also has a peculiar and characteristic pulse, although it is not, as a rule, so readily appreciated as Corrigan's pulse. Unlike the latter which we may visualize, in a sphygmographic way, as a sudden ascent, a sharp peak, and a swift decline, the stenotic pulse conveys the impression of a plateau-like curve. In other words, it takes time to pass the palpating finger. For this reason it is still better felt with two approximate fingers simultaneously. I know of no other condition which will produce this kind of pulse.

The pulse of high blood-pressure.—There is no more characteristic pulse in medicine than the high-tension pulse, the *pulsus magnus, durus, et tardus,* of the older physicians. Unless cardiac defeat has supervened upon long hyperpiesia the pulse is slow and generally of full volume, but what is especially remarkable is the degree of finger-pressure necessary to obliterate the pulse-wave so that it cannot be felt by another finger at a lower level. The artery itself in later stages of the disease imparts a sensation of toughness or hardness to the finger, can be felt and rolled even when the pulse is obliterated, and is commonly tortuous. Accurate estimation of the blood-pressure without the sphygmomanometer is, I believe, impossible even with long practice, but we should generally be able to estimate that a systolic pressure is above 180 or below 100 mm. of mercury. Between these figures it is difficult to arrive confidently within thirty or forty millimetres of the correct reading.

In striking contrast is the extremely *low-tension pulse of Addison's disease* which, when you have had experience of a case or two, may be the first thing to draw attention to the true diagnosis. The symptoms in the early stages of the disease often amount to little more than a complaint of weakness; pigmentation is not always obvious, and in a blonde Saxon type I have known it entirely lacking. There is something arresting and uncanny in the feel of a pulse so weak and compressible in a patient perhaps but recently prevented from going about his affairs. In later stages to palpate is almost to obliterate the pulse. Apart from states of syncope and collapse and certain cases of coronary occlusion, an accident which is usually associated with a pro-

found fall in blood-pressure, it is quite uncommon to feel pulses of the peculiar poor quality which we associate with disorganization of the suprarenal glands, and which Addison himself described as 'small and feeble' or 'excessively soft and compressible'.

There is an alteration in the pulse described as *dicrotism* in which the dicrotic wave is greatly exaggerated and each beat appears to be duplicated or accompanied by a poor reflection of itself. The sensation imparted to the finger is unique, generally unmistakable, and quite distinct from that furnished by a *bigeminal pulse* in which every normal beat is followed by a premature contraction and then by a compensatory pause. It can, however, be mistaken for doubling of the pulse-rate and may be so charted by the nurse. The dicrotic pulse occurs especially in grave febrile illnesses, but is so frequent in typhoid fever and comparatively so infrequent in other diseases that it has long been regarded as a 'diagnostic pulse'.

In a case to which I was called last year, in which severe headache and high pyrexia had led to a fruitless exploration of the accessory sinuses, a dicrotic pulse was noted and was the first thing to suggest the actual diagnosis. I was a little shaken and incredulous when the pathologist, two days later, reported that he had grown *B. coli* from the blood, but we had not long to wait before rose-spots appeared and simultaneously the pathologist revised his verdict and announced *B. paratyphosus B* in all cultures. I have recently had an example of extreme dicrotism in Addison Ward in the case of a boy with miliary tuberculosis with pericarditis. Post mortem we found miliary tubercles throughout the myocardium.

Complete pulselessness, excepting for very short periods or when the artery is obliterated, might be thought to be inconsistent with life. Thus we associate the condition chiefly with syncopal attacks, with shock, haemorrhage, or the moribund state. I have, however, the notes of two cases, in the first of which no pulse could be felt at the wrist for some 12 hours, while in the second the radial, carotid, and subclavian pulses were all impalpable for 12 hours and the

radial was only doubtfully palpable after 24 hours. Both were cases of anaphylactic shock following administration of serum and both made a complete recovery. (See Lecture XXXIII.)

John Hunter records that in his first anginal seizure, which was almost certainly due to a coronary occlusion, four physicians were unable to feel his pulse for the space of three-quarters of an hour. He survived the attack for twenty years. I know of no other conditions in which prolonged pulselessness may occur and yet recovery follow.

A rare pulse anomaly is the *pulsus paradoxus*, in which the pulse weakens or disappears in inspiration. It is n sign of pericarditis with effusion.

The types of pulse which I have endeavoured to describe are all definite in their way and instructive for that reason. Their value is chiefly diagnostic. But there are other less definite pulse-variations, instructive rather in a prognostic way, which it would be beyond my power to describe. How is it that we visit a case sometimes and, notwithstanding that the patient—perhaps a victim of pneumonia or some surgical disease—appears to be doing fairly well, we say 'But I don't quite like the quality of his pulse', and are justified in our anxiety by subsequent events? And how is it, contrarily, that we may see a patient seemingly in dire straits and, largely on the quality of his pulse, give a more hopeful verdict? It is not mere guess-work nor yet any special skill, but rather the interpreted result of past experience and a subconscious reading of rate, rhythm, volume, and tension and their relations to one another and to other signs. Such mental procedures cannot be taught, but it is open to us to acquire them by self-schooling in the art of observation.

Heberden, criticizing certain doctrines prevalent in his time, says:

'I have more than once observed old and eminent practitioners make such different judgements of hard, and full, and weak, and small pulses, that I was sure they did not call the same sensations by the same names. It is to be wished, therefore, that physicians, in their doctrines of pulses, and descriptions of cases, had attended

more to such circumstances of the pulse, in which they could neither mistake nor be misunderstood.'

He was here referring more particularly to the rate, but if we nre clear also in our use and understanding of the terms and systematic in our assessment, when occasion demands, of rhythm, volume, tension, and the condition of the arterial wall, we shall be subscribing still further to this wise behest.

XXII

HYPERPIESIA[1]

We owe to the late Sir Clifford Allbutt, who devoted much time and scholarly labour to the study of arterial disease in general and of arterial hypertonus in particular, the terms 'hyperpiesis' and 'hyperpiesia'. By hyperpiesis we understand the fact of raised blood-pressure; we know that it may be transient or persistent, and that it may accompany a variety of conditions, including arterial disease, chronic renal disease, lesions causing increased intracranial pressure, exophthalmic goitre, and so forth. By hyperpiesia we understand a peculiar and interesting malady in which raised blood-pressure is the most constant and outstanding feature. Clifford Allbutt described it as a malady in which, at or towards middle life, the blood-pressure rises excessively—a malady having a course of its own, and deserving the name of a disease. To Clifford Allbutt we are also indebted for the clearing away of much of the confusion which previously existed between hyperpiesia and renal high blood-pressure on the one hand, and hyperpiesia and senile or 'decrescent' atheroma on the other. In order to prepare the way for our discussion I have tabulated the broader clinical distinctions between these diseases in the later stages of their development.

	Hyperpiesia	*Chronic Interstitial Nephritis*
Age-incidence	40–60	20–50
Physical type	Robust, healthy	Unhealthy, anaemic
Urine	Alb. *nil* or trace	Present, perhaps copious
Cardiac hypertrophy	Always present latterly	Present, latterly
Blood-urea	Not raised or very slightly	Greatly raised
Retinal changes	*Haemorrhages* and 'wiry' vessels	*Albuminuric retinitis*
Death from	*Cerebral haemorrhage* / 'Cardiac defeat'	*Uraemia*

[1] *Guy's Hosp. Gazette*, 1923, xxxix. 540.

	Hyperpiesia	*Senile or 'Decrescent' Atheroma*
Age-incidence	40–60	60–80
Artery	Thick, tough, but not at first tortuous	Thick, hard, tortuous
Blood-pressure	*Always raised*	*Not necessarily raised*
Heart	Hypertrophied	Not necessarily hypertrophied
Death from	Cerebral haemorrhage 'Cardiac defeat'	Coronary arteriosclerosis with myocardial degeneration, or intercurrent disease

The Causes of Hyperpiesia

Is the high blood-pressure in hyperpiesia due to arterial disease, or is the arterial disease due to the high blood-pressure? That the high pressure is not wholly due to the arterial disease is apparent from the fact that periods of great improvement may occur in the course of the malady, and also from the observation that the blood-pressure may be temporarily and greatly lowered by the administration of nitrites. In other words, even if arterial disease be present from the beginning—which is doubtful—we must also imagine the presence of some other factor which raises blood-pressure by stimulating hypertonus of the arterial musculature. It is commonly supposed that some circulating pressor substance is at work, and disputes occur as to whether this pressor substance is in the nature of a toxin resulting from bacterial action within the body, or whether it is a product of faulty metabolism, or otherwise evolved. Against the bacterial theory are the observations that most bacterial toxins have a depressor effect, and that sufferers from hyperpiesia are commonly robust and healthy looking individuals with no discoverable sign of alimentary or other intoxication.

Various careful researches have shown that in cases of hyperpiesia examined after death there is present in the arteries, and more in some arteries than in others, a definite and constant histological change. To this change Dr. Geoffrey Evans has given the name *diffuse hyperplastic sclerosis*. His work would seem to suggest that diffuse hyperplastic sclerosis is the pathological synonym for the clinical

condition hyperpiesia. He gives as the most reliable clinical evidence of hyperpiesia a systolic blood-pressure of (or above) 190 mm. of mercury; and as the most constant and prominent morbid anatomical finding cardiac hypertrophy, with a heart usually weighing over 15 oz.

I would not have you *imagine* from this that hyperpiesia cannot be diagnosed in the presence of lower blood-pressures and in the absence of clinically obvious cardiac hypertrophy. The disease should be diagnosed, if the patient presents himself soon enough, long before such a stage has been reached. We do not really know whether or not diffuse hyperplastic sclerosis is present in the early phases of the disease, but we do know that clinically the radial artery may at first show very little thickening or hardening.

Setting aside for the moment all theories in regard to the existence of a pressor substance, are there any other observations which suggest the existence of other causal or contributory factors in the development of hyperpiesia? The older physicians, having no bacteriologists or biochemists to instruct or bewilder them, devoted much time to the study of aetiology and diathesis. From such studies they often drew valuable conclusions, and in few chronic diseases does study of this kind prove more profitable than in the case of hyperpiesia. Thus we find evidence of a predisposition to hyperpiesia both in family history and in physical type, and it has long been recognized that there is a very definite age-period at which symptoms appear, and within which the course of the disease is laid. It is not at all rare to find that cerebral haemorrhage or heart failure has been a common cause of death among the relatives or ancestors of a patient with high blood-pressure, and that these deaths have for the most part occurred between the ages of fifty and seventy. The majority of sufferers from hyperpiesia are of rather a robust and vigorous type, sometimes plethoric, sometimes obese, although I think we should also include a lean and nervous type. For the purposes of this lecture I at one time looked through the notes of all my patients with high blood-pressure. From these I excluded all cases in which the high blood-pressure was due to other apparent causes,

such as nephritis or Graves's disease, all cases in which the patient presented himself on account of another disease, and all cases in which the high pressure might have been a transient phenomenon, or in which other symptoms or signs of hyperpiesia were lacking. The systolic blood-pressure was 170 or over in every case and the diastolic pressure 100 or over in all cases but one, cases with lower figures being excluded for purposes of the survey. I obtained the following figures in regard to age-incidence and physical type:

	Males, 46%	*Females, 54%*
Age—Lowest	21	28
Highest	68	72
Average	57	53

Physical Type (both sexes together)

Robust, healthy, stout, plethoric, or 'hypersthenic'	62 per cent.
Average	18 ,,
Lean and nervous	4 ,,
Poor physique	16 ,,

Other factors besides the family history, age, and physical type which are commonly associated with hyperpiesia are the menopause in women, at which period high-pressure symptoms may manifest themselves rather abruptly; hard work; worry; the stress of modern life; and good living. The part played by tobacco and alcohol is doubtful. The information available thus suggests that hyperpiesia should at present be regarded rather as a reaction to various morbid stimuli, and occurring in individuals of the hypersthenic constitution, than as a specific response to a single specific substance. If a pressor substance is necessary for the production of the arterial hypertonus, perhaps we might suggest that this substance is activated through the sympathetic nervous system sometimes by over-eating, over-work, or worry, sometimes by the endocrine disturbances of the menopause or by a combination of these factors, but that such activation is seldom effective unless there is already present a constitutional or diathetic factor.

Clinical Features and Course

The symptoms which may be complained of by sufferers from hyperpiesia are very numerous, but for the most part

they have reference to the head or the heart. In the early stages these symptoms may appear trivial and unconvincing and unless the blood-pressure be taken—and the sphygmomanometer must be the arbiter in every suspected case—the diagnosis may well be missed at a stage in which the prospects of treatment are most favourable. On the basis of my case-notes I have tabulated the main symptoms exhibited amongst a group of patients who were for the most part sufficiently well to be up and about and leading moderately active or partially restricted lives. The few exceptions were cases of cerebral haemorrhage or failing heart. The frequency of the symptoms in the series is given as an approximate percentage:

Main Subjective Symptoms

	Per cent.
Headaches, including pressure feelings, 'bursting sensations', 'tight band round head', &c.	45
Cardiac symptoms (including dyspnoea, precordial pain, consciousness of heart throbbing)	33
Nocturnal frequency	32
Dizziness	26
Nervousness (including anxiety, fears, claustrophobia)	22
Fatigue	18
Anginal pain	10
Cerebral vascular lesions (symptoms of)	10
Ocular symptoms, including sudden blindness, failing vision, effects of intra-ocular haemorrhages	8
Epistaxis	6
Mental symptoms	6
Noises in head	6
Haemoptysis	4

It will at once be observed that many of these symptoms, such as headache, dizziness, dyspnoea, and nervousness are common to a host of other diseases, and that many of them may also occur in patients without any appreciable evidence of organic disease at all. The list should, however, serve to remind you how important it is never to neglect subjective symptoms; and perhaps this is particularly the case about the middle period of life. The majority of these symptoms sufficiently explain themselves. The cardiac symptoms are a direct result of over-working of the left ventricle in its effort to combat the increased peripheral resistance. The nocturnal frequency is probably due to the high pressure in

the renal arterioles; the headaches and dizziness to increased intracranial pressure; the anginal pain to local sclerosis of the coronary arteries; the fatigue symptoms to combined cardiac and cerebral over-stimulation and over-activity; the epistaxis to a rupture of the delicate unprotected capillaries of the nasal mucosa. The nervousness, however, requires more judicial consideration, for in some cases it is very difficult to say how far a nervous and anxious mind has predisposed to the hyperpiesia, or how far the hyperpiesia has rendered the patient more liable to emotional unrest. I have small doubt that high blood-pressure can create in a previously calm and phlegmatic individual a state of mind in which he is easily perturbed or 'rattled', and in which 'molehills' take on the proportions of 'mountains'.

Physical examination commonly shows the sufferer from hyperpiesia to be a vigorous type of man or woman, sometimes looking so healthy that the facial aspect misleads into an attitude of false security. A little later in the course of the disease the red cheeks may show an underlying tinge of purple, particularly in cold weather. In the hyperpiesia accompanying the menopause there is a liability to a diffuse and sustained flushing of the face and neck during moments of anxiety or fatigue, which is, I think, an aggravation of the ordinary 'hot flushing' complained of at these times. The pulse is full and slow and not readily compressible—the *pulsus magnus, durus, et tardus* of the old physicians. The quality of resistance imparted to the fingers by the artery is often that of toughness rather than hardness. The apex-beat may be found to be in or perhaps just to the left of the nipple line. The aortic second sound is accentuated, sometimes sharp or sometimes ringing. The fundi may show wiry and rather tortuous vessels, perhaps even a small haemorrhage or two. At an early stage the arteries compress the veins as they cross them. The urine is of low specific gravity, and it may or may not show a trace of albumin.

It is difficult to estimate the average duration of the disease, for we do not in any individual case know when it began, and the onset and progress are insidious and the course variable. Perhaps some idea of its natural stages may

be given by providing you with a composite picture of a case: A hard-worked business man discovers at fifty that his pulses go a little too quickly, and that he has slight shortness of breath on exertion, that he has become liable to mild temporal headaches, and that he tires more easily than he used to do. Odd symptoms of a minor kind may be traced back a year or two earlier. His blood-pressure is found to be 160 systolic, 110 diastolic. His urine shows a faint haze of albumin on boiling. He continues with his work, taking rather more care of himself than before, and a year or two later, after a busy spell, reports himself as rather more troubled with dyspnoea, and mentions occasional bouts of epistaxis. During this time his blood-pressure is found to have risen to 200 systolic, 130 diastolic. He has become rather irritable; has to get up to pass water twice at night; and is annoyed by being unduly conscious of his carotid pulsations when he lays his head on the pillow. He is persuaded to retire from his work and to lead a quieter life. For a time he shows definite improvement, but ultimately, after a longer or shorter interval, is carried off by a cerebral haemorrhage, or sometimes less abruptly by what Clifford Allbutt so aptly describes as 'cardiac defeat'. The period which elapses between his first symptoms and his death may be anything between five and fifteen years or even longer; the symptoms experienced during that time may be slight or troublesome or only latterly crippling. Often the response of the hypertrophied heart is good throughout, and, without any urgent or distressing symptoms ever having developed, death kindly closes the scene with a sudden apoplexy. But there is a rosier side to the picture, for some patients will support a systolic blood-pressure of 180 or 200 for years, leading contented and even active lives and dying of some other disease. Indeed high arterial pressure only becomes of serious moment when it begins to produce symptoms of distress and signs of structural damage in other departments of the body.

This lack of definite correlation between the height of the recorded pressures and the severity of symptoms brings us necessarily to the discussion of what is a pathological

high blood-pressure. Various methods are given for assessing the average blood-pressure at different ages. A simple plan is to take the systolic pressure as 120 at the age of 20 and to add ten millimetres of mercury for each decade, but some observers regard all blood-pressures above 150, whatever the age of the patient, as pathological. I should regard a systolic blood-pressure of 180 or upwards as pathological and signifying hyperpiesia at any age, but I am satisfied that it is quite possible, in the presence of other symptoms, to diagnose hyperpiesia correctly with a blood-pressure of 160. I should be disinclined to diagnose hyperpiesia with a blood-pressure below 150, excepting in a young subject, or with a clear association of other confirmatory signs and symptoms. With the more doubtful borderline figures repeated observations with the sphygmomanometer should always be made. The diastolic pressure was 100 or over in every case but one in my series, and 110 or over in four-fifths of the series.

Differential Diagnosis

As I have already shown, the differential diagnosis must be made particularly from chronic interstitial nephritis, and in the presence of retinal changes, much albumin, or other suggestive features, the blood-urea should be estimated, or other renal efficiency tests performed. High blood-pressure in young subjects should also be more carefully studied from the renal point of view than at the more usual age-period for the disease. The list of symptoms which I have given will remind you that care may be necessary to distinguish the earlier phases of hyperpiesia from anxiety states, from neurasthenia, and from simple over-work. A small haemoptysis with fatigue symptoms may raise a suspicion of pulmonary tubercle. When the heart becomes enlarged and murmurs develop, the differentiation from primary cardiac disease must also be made. Of all the causes of organic heart-disease hyperpiesia is the commonest. In a patient of middle age with no previous history of rheumatic or syphilitic infection, the development of cardiac symptoms

or signs should be an immediate signal for blood-pressure observations.

Prognosis[1]

Enough has already been said to show you that prognosis is difficult in the early or middle periods of the disease; but when serious vascular lesions or cardiac failure develop, the outlook is obviously bad. With the slighter symptoms and objective signs of cardiac involvement or repeated small vascular lesions the forecast must needs be guarded. If, however, the case be seen in the early stage, when symptoms rather than signs give the clue to the diagnosis, and if a suitable way of life can be enjoined, the outlook may be quite good, although longevity is not probable. A high blood-pressure discovered independently of other symptoms or signs of hyperpiesia in the course of a routine examination should be confirmed by further observations, and does not necessarily demand a gloomy forecast. A very high diastolic pressure is relatively of more serious import than a high systolic pressure. A case occurring at the menopause may sometimes improve greatly when this phase of life is past. The patient's fitness in other ways, his mode of life and his family history must, of course, always be taken into account, for prognosis, like diagnosis, should invariably be based upon a careful general survey. It need hardly be added that to the patient himself as good a prognosis as possible should be given, provided it does not so enhance his sense of security as to make him neglectful of his therapeutic rules.

Treatment

It might at first seem hopeless to suggest remedial measures for so insidious and seemingly so relentless a disease, but *in point of fact, a great deal of good may be done in little ways.* Medicines play a small part only in the treatment. Nitrites should not be prescribed excepting for the treatment of such urgent symptoms as anginal pain. Iodides are said to reduce the pressure but are of uncertain value, and it should probably be our aim rather to check or delay the further rise of pressure

[1] *Vide* also Chapter XX.

than to produce a fall. A restful life, where possible, with avoidance of physical and still more of mental fatigue; avoidance of hurry, worry, and flurry; a dietary régime tending, but not too strictly, towards the vegetarian; good holidays; and reassurance and bromides for the anxious-minded patients, all play their part. The consumption of tobacco and alcohol should be kept within reasonable limits, and the latter, if previously taken to excess, forbidden. Weight reduction in obese cases is valuable, and produces more subjective and objective improvement than any other single measure. Never tell the patient his actual blood-pressure readings. Periodic venesections in the plethoric type of hyperpietic patient have been recommended, in the old days were much practised, and would seem rational, but the results are not lasting. With hyperpiesia, as with every other disease, early diagnosis is the most important hand-maid of treatment. I would therefore urge you to familiarize yourselves with subjective symptoms, however trivial, and always to try to find for them a reasonal interpretation. You should also practise your fingers, your stethoscopes, and your ophthalmoscopes assiduously. Examine all radial arteries with care, and register the systolic and diastolic blood-pressure with the sphygmomanometer in every case in which it falls to you to perform a routine overhaul. The forefinger may readily learn to judge the presence of very high and very low pressures, but with figures between 110 170 mm. of mercury it is impossible to be accurate.

Finally, for its historical value and associations, it is of interest to consult an article entitled 'Some of the Clinical Aspects of Chronic Bright's Disease', in the *Guy's Hospital Reports* for 1879, by Dr. Mahomed, then Medical Registrar, and later Assistant Physician to Guy's Hospital. Without the aid of the sphygmomanometer, which was not then invented, but with the aid of the sphygmograph, Dr. Mahomed was among the first to throw light upon the importance of blood-pressure observations in disease, and to predict much that has since been established in regard to this interesting and prevalent malady.

XXIII

'CHRONIC BRIGHT'S DISEASE WITHOUT ALBUMINURIA'[1]

AN HISTORICAL NOTE ON THE CONTRIBUTIONS OF *BRIGHT AND HIS SUCCESSORS OF THE GUY'S SCHOOL* TO THE STUDY OF HIGH BLOOD-PRESSURE AND ITS CONSEQUENCES

It is clear from a perusal of Bright's writings on the disease which bears his name, and notably from a study of the cases included in his 'Tabular View of the Morbid Appearances in 100 Cases connected with Albuminous Urine',[2] that his descriptions were concerned with several varieties of renal damage. This he undoubtedly appreciated himself, but for the most part he was content to record his observations upon them and refrained from advancing theories of their relationships and origins. Gradually others who followed him, and not least among these certain physicians of the Guy's school, helped to differentiate, both anatomically and clinically, the several forms of 'morbus Brightii'.

The form of the disease with which this note is concerned is that which has now come to be regarded (largely through the researches of Wilks, Gull, and Mahomed) as primarily a disease of the arterioles and capillaries and only secondarily of the kidneys. In this disease the most outstanding and constant clinical feature is an excessive rise in the arterial blood-pressure; the most outstanding pathological features are the presence of certain changes in the vessels, originally described by Gull as 'arterio-capillary fibrosis', and of cardiac hypertrophy. In Bright's 'Tabular View' there are records of several patients in the middle period of life who are shown to have succumbed to cerebral haemorrhage or heart failure, and in whose post-mortem findings are reported kidneys 'small, hard and granulated', and hearts showing 'great hypertrophy of the left ventricle'. These

[1] *Guy's Hospital Reports* (Bright Centenary Number), 1927, lxxvii. 307.
[2] *Guy's Hospital Reports*, 1836, i. 350.

cases were evidently distinct from those in which death occurred, usually at an earlier age, with anasarca or uraemia, and (employing the modern clinical terminolgy suggested by Sir Clifford Allbutt) may be accepted as examples of 'hyperpiesia' in its latest stage.

The story of high blood-pressure and its consequences may therefore be said to have started with the final chapter, for Bright concerned himself almost entirely with its morbid anatomy and terminal morbid physiology. He was only indirectly responsible for the chapters added later by others working under the inspiration of his pioneer studies. Nevertheless, while principally concerned with the demonstration of the renal changes and of the frequent associatioa of albuminuria, Bright was very much alive to the coincidence of damage in other organs, and especially in 'the circulating system'. The cardiac hypertrophy attracted his attention, and the hard pulse, which had loag been a familiar accompaniment of apoplexy, became associated at this time with the more general pathological picture which he painted. In so far as he allowed himself to consider causes Bright wrote with customary caution, and while naturally inclined, in the light of his discovery, to regard the kidney as prime offender, he was far-seeing enough to remark, '. . . yet we are not at liberty to assume that the disease of the kidney has been the primary cause on which the disease of the rest depended'. When discussing the structural changes in the heart he is equally guarded, and, commenting upon the frequency of hypertrophy without valvular disease, he continues: 'This naturally leads us to look for some less local cause for the unusual efforts to which the heart has been impelled; and the two most ready solutions appear to be, either that the altered quality of the blood affords irregular and unwonted stimulus to the organ immediately; or, that it so affects the minute and capillary circulation as to render greater action necessary to force the blood through the distant subdivisioas of the vascular system.'

Beyond these observations and opinions we can trace little in Bright's papers which seems to have a direct hearing on the problem of arterial disease and high blood-pressure,

but when we consider that his researches formed the groundwork upon which the investigations of Wilks, of Gull and Sutton, and of Mahomed were founded, they assume an additional importance and remind us that 'morbus Brightii' was a discovery which cast its illumination over far more than the renal tubules and added not one but several new chapters to the book of medical knowledge.

Reviewing the writings of those who followed him, it would seem that, for more than fifty years after his last publications on renal disease and albuminuria, chronic Bright's disease was held especially to imply that malady of middle life which clinicians of a later generation have labelled variously as arteriosclerosis or hyperpiesia, and pathologists as arterio-capillary fibrosis, arteriosclerosis, or, more recently, diffuse hyperplastic sclerosis. In the earlier stages of its history that form of the disease which we now call 'chronic interstitial nephritis' was apparently not separately identified.

In 1852 Sir Samuel (then Doctor) Wilks contributed a long article to the *Reports*, entitled 'Cases of Bright's Disease, with Remarks'.[1] He notes that albuminuria is not invariably a symptom of chronic Bright's disease, and vividly contrasts a case of acute dropsical disease in a young woman presenting large white kidneys at autopsy, with an almost symptomless case of sudden death in an old man whose kidneys were found to be small and red and hard. Several of the descriptions in the appended list of 33 cases belonging to this second group refer to examples of 'hyperpiesia' with death by 'cardiac defeat' (Clifford Allbutt) or by cerebral haemorrhage. Wilks also comments upon the variety of complaints with which sufferers from chronic Bright's disease present themselves, none of them necessarily incriminating the kidney, and remarks that 'the condition of the artery on *feeling* the pulse often leads to the suspicion of the disease, a thickened tortuous artery occurring so frequently in "morbus Brightii"'. Furthermore, in respect of the findings after death, he is struck by the invariable presence of arterial disease in those cases which

[1] *Guy's Hospital Reports* (2nd Series), 1852, iii. 232.

show cardiac hypertrophy. Beyond hinting at the possible influence of senescence and alcoholism and discountenancing the influence of gout and scrofula he has little to suggest in respect of aetiology.

Twenty years later Sir William Gull, writing in conjunction with Dr. H. G. Sutton, gave to the world his classical account of 'The Pathology of the Morbid State commonly called Chronic Bright's Disease with Contracted Kidney'.[1] As the result of careful anatomical and histological researches he established the disease for the first time as one of the arteries and capillaries, and stated his conclusions as follows:

'(1) There is a diseased state characterized by hyaline-fibroid formation in the arterioles and capillaries.

'(2) This morbid change is attended with atrophy of the adjacent tissues.

'(3) It is probable that this morbid change commonly begins in the kidney, but there is evidence of its also beginning primarily in other organs.

'(4) The contraction and atrophy of the kidney are but part and parcel of the general morbid change.

'(5) The kidneys may be but little if at all affected, whilst the morbid change is far advanced in other organs.

'(6) This morbid change in the arterioles and capillaries is the primary and essential condition of the morbid state called chronic Bright's disease with contracted kidney.

'(7) The clinical history varies according to the organs primarily and chiefly affected.

'(8) In the present state of our knowledge we cannot refer the vascular changes to an antecedent change in the blood due to the defective renal excretion.

'(9) The kidneys may undergo extreme degenerative changes without being attended by the cardiovascular and other lesions characteristic of the condition known as chronic Bright's disease.

'(10) The morbid state under discussion is allied with the conditions of old age, and its area may be said hypothetically to correspond to the "area vasculosa".

'(11) The changes, though allied with senile alterations, are probably due to distinct causes not yet ascertained.

'Should it be considered necessary to distinguish this morbid state by any special term, we venture to suggest for the purpose the name "arterio-capillary fibrosis".'

[1] *Medico-Chirurgical Transactions*, 1872, lv. 273.

Gull goes farther than Wilks, who found that albumin was not necessarily present in the urine, for he shows that the kidneys themselves may show no gross changes. The sufferers from the disease he finds, as has always been remarked, principally at or after middle life and very rarely in youth. Ever insistent on the importance of 'the general view', he concludes a clinical lecture[1] on the subject of arterio-capillary fibrosis, given at Guy's Hospital, in the following dramatic sentences:

'It is always dangerous to rest in a narrow pathology; and I believe that to be a *narrow pathology which is satisfied with what you now* see before me on this table. In this glass you see a much hypertrophied heart and a *very contracted kidney. This specimen is classical.* It was, I believe, put up under Dr. Bright's own direction, and with a view of showing that the wasting of the kidney is the cause of the thickening of the heart. I cannot but look upon it with veneration, but not with conviction. I think, with all deference to so great an authority, that the systemic capillaries, and, had it been possible, the entire man, should have been included in this vase, together with the heart and the kidneys; then we should have had, I believe, a truer view of the causation of the cardiac hypertrophy and of the disease of the kidney.'

Improvements in histological technique and staining methods may have modified or corrected their more detailed opinions, but the general conception of Gull and Sutton remains uncontroverted.

We pass next to a review of some remarkable contributions written from the clinical standpoint. I refer to the papers by Dr. F. A. Mahomed which appeared in various journals between the years 1874 and 1881, and of which the more important are to be found in the *Guy's Hospital Reports* for the years 1879[2] and 1881.[3] From the second of these, which was submitted as a thesis for the degree of M.B. in the University of Cambridge, I have borrowed the title of the present memoir. The title and the paper leave no room for doubt that Mahomed was concerned with the description of what we now call 'hyperpiesia'. Sir Clifford Allbutt in

[1] *Brit. Med. Journ.*, 21 Dec. 1872
[2] 'Some of the Clinical Aspects of Chronic Bright's Disease.'
[3] 'Chronic Bright's Disease without Albuminuria.'

his work on *Diseases of the Arteries* pays tribute to Mahomed's work, but I cannot help feeling that many other writers on the subject of high blood-pressure have done but scant justice to his painstaking researches. Mahomed may be regarded as one of the chief pioneers of blood-pressure observations in disease. He had no sphygmomanometer such as we possess, but with the aid of his fingers, his own modification of Marey's sphygmograph, and the roughest methods of measuring pressures, which he expressed in terms of ounces, he amassed records and marshalled arguments which are a monument to his zeal and industry and brilliant intellect. More clearly than any one previously he defined clinically that form of Bright's disease which tends to terminate with apoplexy or heart-failure. Having established what he called a pre-albuminuric phase of the disease, he then showed that albumin could be absent in all stages, and when present terminally that this was sometimes an effect rather of heart-failure than of renal damage. He showed that in the absence of albuminuria the disease could be readily diagnosed by observation of the symptoms, the pulse, and the position of the apex beat, and by careful analysis of the type of tracing obtained with the sphygmograph. He sought to explain the various qualities of the *pulsus magnus, durus et tardus* of the old physicians on the basis of his sphygmographic findings. He accounted reasonably for many of the symptoms of high blood-pressure and described, with much attention to detail, the ways in which the heart may fail. He illustrated graphically some types of peculiar cardiac rhythm which he encountered in cases of heart-failure due to high arterial pressure, employing not only sphygmographic records but simultaneous records from the radial and jugular pulses and the apex beat. He discussed the murmurs of heart-failure in chronic Bright's disease and showed that, while simulating the murmurs of valvular disease, they were not due to valvular lesions, paying particular attention to the presystolic murmur not infrequently heard in cases of pronounced cardiac dilatation. He pointed out that while the 'red' contracted kidney could be unaccompanied by albuminuria, the 'yellow' or

'mixed' contracted kidney gave albumin and a urine generally of lower specific gravity. He showed that in scarlatina the blood-pressure rises before the development of albuminuria or other evidences of nephritis. He put in a plea for the view, still maintained by many, *that high blood-pressure precedes and may cause arterio-capillary fibrosis*, and argued that the high pressure could not be attributed solely to organic arterial changes, since Broadbent had demonstrated a reduction of high pressure with amyl nitrite, presumably by arterial relaxation. He insisted that high arterial tension and not albuminuria should be accepted *as the sign* of chronic Bright's disease. He emphasized the possibility and importance of early diagnosis. He found high pressures in a small percentage of young people, and discussed 'the recognition of the Diathesis in young persons during health and previous to structural change', and in further support of the influence of constitution adduced the high incidence of apoplexy in some families. And finally, notwithstanding the changes of view for which he himself was partly responsible, he loyally insisted on the retention of 'chronic Bright's disease' as the most fitting nomenclature.

If we except the comparatively small additions to our knowledge which have accrued through perfected technical and instrumental aids—that is to say, through the agency of the sphygmomanometer, better interpretation of ophthalmoscopic appearances, improved histological methods, and the arrival of new methods of testing cardiac and renal function—we may, I believe, justly claim that the whole of the story of high blood-pressure, including the little we know of its aetiology and the great deal we know of its consequences, was written at Guy's between the years 1827 and 1881.

Other causes of 'hyperpiesis'—physiological and emotional, or expressing increased intracranial pressure or an over-active thyroid gland—have been revealed, but there is only one 'hyperpiesia,' and that is chronic Bright's disease without (and sometimes with) albuminuria. For the history of this disease Bright, Wilks, and Gull provided the pathological and later clinical chapters, while Mahomed completed the clinical episode in all its phases.

Of prime causes—however much we may speculate about a 'pressor substance'—we know no more to-day than they did; of prognosis and treatment very little more.

Bright's influence on medical thought and teaching at Guy's has made itself felt in successive generations and in various ways; partly through the lustre of his name and achievement and partly through his initiation, in concert with Addison and Hodgkin, of a famous line of physician-pathologists, with its tradition of faithful observation and record at the bedside, pursued and completed, whenever possible, in the post-mortem room.

The purpose of this brief memoir has been to indicate how, in a more direct manner, the researches of Richard Bright provided a basis and inspiration for subsequent investigations of permanent value, carried out within the same precincts and in accordance with his own sound principles, on the predominant variety of his own disease.

XXIV

ANGINA PECTORIS AND ALLIED SEIZURES[1]

In the list of diseases with which we go armed in practice there are a few which stand apart by reason of some peculiar interest or importance attaching to them, or of the urgency of the situations which they create. Of such are typhoid fever, syphilis, pneumonia, and the abdominal emergencies, but none, perhaps, make a stronger appeal to the mind than those cardiovascular disorders which have as their major manifestation the dreaded breast-pang. Since Heberden, in 1768, painted for us with simple, vivid phrase the clinical picture of angina pectoris, it has always claimed the attention and stirred the curiosity of physicians. The reasons are not far to seek. A fully developed anginal attack, even in the narrative, and how much more in the witnessed event, is a drama in itself, and, all too often, prophetic of human tragedy. On the academic side we are faced with the ever-present difficulties of explaining the phenomena and forecasting the issue of the attacks, which frequently arrive in the midst of apparent health and in the absence of gross evidences of disease. For these reasons, and because pain has always seemed to me to be one of the most necessary and fascinating studies open to the practising part of our profession, I decided that the pain of pains, and some of its near congeners, would make a fitting topic for discussion. I shall confine myself to a consideration of—

1. The clinical features of the anginal syndrome.
2. Its clinical varieties and their significance (for it is most important not to regard angina as expressive of any single pathology).
3. Some other conditions which bear a close resemblance to it.

By my descriptions I shall endeavour to suggest some working views in respect of the classification of cases, the

[1] *Clinical Journal*, 1927, lvi. 613.

nature of the symptoms, and the prognosis in the several disorders of which these symptoms are eloquent.

Aetiology and Pathology

In regard to aetiology and pathology let it suffice to say that angina pectoris, taking the graver forms, occurs mostly at or after the age of 50, and that it is much more common in men than women; but that, taking all forms, it may occur at any period of adult life and is fairly evenly distributed between the sexes; that it is frequently—but not invariably—associated with changes in the arteries and particularly—though not necessarily—with atheroma of the first part of the aorta and the coronary vessels; that in younger subjects it may be associated with syphilitic aortitis; and that 'nervous', 'anaemic', and 'toxic' varieties, without demonstrable organic change, are also encountered. The fact that it has so many and such varied associations at once suggests the impropriety of regarding angina pectoris as a disease. It is not a disease but a syndrome (or group of symptoms), and yet such a dramatic syndrome that it assumes the importance of a disease in our minds.

The Pain

Now the main symptom is indubitably the pain, and it is a pain of such a peculiar kind and often of such severity that it merits special study. It will be generally conceded that the pains of visceral disease in which physical signs are scanty or altogether lacking require a more searching analysis than those with clear objective associations. It is, I believe, a good plan to employ some definite scheme of analysing such pains. I would suggest that our interrogatory should include ten questions (*vide* Lecture III). Of these two have reference to quality and quantity, and may be answered under the headings of *character* and *severity*. Three have reference to the location or spacial relationsbips of the pain, and may be answered under the headings of *situation*, *localization* (or *extent of diffusion*), and *paths of reference*. Three have reference to temporal relationships, and may be answered under the headings of *duration*, *frequency*,

and *particular times of occurrence*. Two have reference to determining causes, and may be answered under the headings of *aggravating* and *relieving* factors. Over and above all these our inquiry must, of course, include *associated symptoms*.

Let us apply these questions in the case of the pain of angina pectoris. Of its *character* in bad cases we might almost say that it defies description, but it is generally recorded as a crushing, bursting, constricting, or vice-like pain. In *severity* it varies from a mere sense of discomfort or oppression—often at first it is mistaken for flatulence—to the extremest agony that man is called upon to suffer. Of its *situation* we may say that it is generally retrosternal, but it may be as high as the manubrium, as low as the ensiform, or even epigastric. Sometimes it is situated to the left and lies within the praecordial zone. Its *localization* is fairly confined and accurate, and may be indicated with a closed fist held against the sternum, but its possible *paths of reference* are numerous and wide. Most common and characteristic is the reference down the inner side of the left arm to the elbow, or as far as the ring and little fingers of the left hand; but it may also pass into the right arm, up the side of the neck, or into the jaw. The *duration* of an anginal paroxysm, induced as it usually is by some physical effort, is a matter of minutes rather than seconds or hours, but it is common for the attacks to become more prolonged with the passage of time. The *frequency* of the paroxysms is very variable. A man may die in his first attack, or survive it for many years with frequent attacks or with long freedom from pain. Generally speaking, they tend to become more frequent and to arrive for lesser causes. Of *particular times of occurrence* Heberden is careful to mention the early hours of the morning after the first sleep, when other 'spasmodic complaints' are liable to assert themselves. Of *aggravating causes*, physical efforts such as walking up a slope (especially 'on a full stomach'), anger, anxiety, and cold are all noteworthy. Peace of body and mind, warmth, and, in the attacks, absolute immobility and amyl nitrite are the main *relieving factors*. Of *associated symptoms* the 'angor animi' is the most remarkable, but only occurs in about 20 per cent. of

cases. It is sometimes referred ta as 'the fear of impending death'. More correctly it is an actual 'sense of dying', and sometimes more awful in its effect upon the patient's mind than his physical sufferings. A sense of restricted breathing (but without dyspnoea), tingling and numbness (instead af pain) in the arms, and palyuria after the attack may also be mentioned. Between attacks the patient at first feels well and may appear ta be in robust health. Shauld heart-failure with arrhythmia or congestive signs supervene the attacks may altogether disappear. Summarizing the features af the anginal seizure in a single brief definition, we may say that it is '*a substernal pain of cardiovascular origin, paroxysmal in character, sometimes of great severity, most constantly induced by effort and relieved by rest, and in some cases associated with a peculiar sense of dying*'. 'Heart-attacks' withaut pain and not canfarming in some af the main particulars with this descriptian cannat be certainly regarded as anginal, and when we came ta eansider the peripheral 'allied seizures', these, tao, should show analagaus eharacters.

The Clinical Varieties

I wauld next ask your eansideratian af the clinical varieties af angina pectaris, and in this I may perhaps best help by selectians fram my case-nates, sa arranged as to give pictures, first af the more innacent, then af the less innacent, and finally of the gravest forms. At this point, too, I wauld ask yau to decide whether we should continue to employ ar finally reject the term 'pseudo-angina'. I would plead for its rejection, or for its retention anly as an instrument for reassuring an anxious patient afflicted with what he ar she has regarded as a grave, but what we believe to be an innocent, angina. It may he true that the more innocent forms are commoner in wamen, and occur at an earlier age; but if the symptoms have a genuine relationship ta those included in our definition they are surely 'anginal'. When a patient has hunger-pain from excessive smoking or worry, we do not say that he bas pseudo-hunger-pain because he lacks a duodenal ulcer. Surely it were better to speak of benign and malign angina rather than af false and true

angina, for, from a practical point of view, what we have to decide in the individual case is—'Is this a form of disease about which I can give a reassuring prognosis, or is it one which may sooner or later cause the patient's death?'

Before discussing even the most innocent clinical variety of anginal seizure let us ask ourselves—and it is a useful question to ask of any subjective symptom—whether there is anything in health closely or remotely akin to it. I think there is. Confronted one day at my Out-Patients by an elderly man with a history of severe anginal attacks, I asked him to give us as clear an account as he could of what the symptoms were like. His reply was: 'Well, sir, you know as a young man what it felt like when you tried to run a race *untrained*—the awful, *tight*, bursting *feeling in your chest*. It is like that, but a hundred times worse.' That was a good observation, and you will note that it was the tight, bursting sensation and not the dyspnoea to which he referred. The anginal distress, or something akin to it, can be evoked by a supernormal effort in a healthy person; in an unhealthy person it may be evoked, and with magnified intensity, by a slight effort.

Case 1. I was consulted for a transient dry pleurisy by a healthy-looking woman, aged 30. After describing her present symptoms she mentioned quite casually that for as long as she could remember, whenever she went out for a walk on a cold day she had had a pain in the chest which radiated down the left arm. In every other way she was perfectly well, and she led an active life. There were no signs of cardiovascular disease. There was clearly no anxiety about her case, and yet her vasomotor responses to cold combined with effort were adequate for the production of minor anginal pain with a typical reference.

Case 2. A woman, something under 40, came on account of several attacks within a period of 6 months, characterized by a severe pain behind the sternum, radiating down the left arm to the little finger, which remained numb when the attacks had passed. She also had a feeling as though she were going to die. The attacks generally came on when she was tired. She was 'run down' and unfit, had suffered a great emotional stress, and was working too hard. She had had some minor rheumatic symptoms, but there were no signs of organic disease of the heart or arteries, and her blood gave a negative Wassermann test. With rest and reassurance she steadily improved. I

regarded hers as a case of benign angina dependent on vasomotor disturbances and not on structural cardiovascular disease.

Case 3. It was less easy, although I elected to do so, to give a reassuring verdict in the case of a woman, aged 52, who complained of a pain behind the lower sternum induced by walking up hills, or against the wind, or by sudden cold, or by stooping. The pain was always relieved when she stood still. It frequently radiated to the left wrist. In every other respect she felt perfectly well. The important additional piece of evidence was that *she had had the symptom for 17 years*. It developed at a time of great mental anxiety, when a domestic disruption had necessitated her taking upon herself physical and mental burdens and responsibilities beyond what should be expected of any woman. To make prognosis still more difficult she had a blood-pressure of 150 systolic, 90 diastolic, and possibly slight hypertrophy of the left ventricle. What were the chances of her benign angina becoming malign with the development of organic arterial changes as her age advanced?

Case 4. In the next case, more typical of Heberden's description, the prognosis was clearly bad. A man of magnificent physique, aged 67, complained of a gripping pain behind the lower sternum on mounting hills or stooping and after food. It had also caught him on getting into bed—probably through the contact of the cold sheets—and had occasionally wakened him at 2 a.m. It passed down both arms to the elbows. In a minor form he had been occasionally aware of it for 5 years. His blood-pressure was 205 systolic, 110 diastolic, and his urine showed a trace of albumin. The attacks were becoming more severe and frequent.

The severity or slightness of the pain is, however, of no certain prognostic import.

Case 5. An old clergyman who had led a healthy and active life complained of a 'bursting' feeling behind the sternum, always induced by walking and associated with tingling in the left arm. There was no agony and no angor animi. His radial artery was slightly thickened; his blood-pressure was 180 systolic, 110 diastolic; his apex beat was in the nipple line; he had frequent extra-systoles. He was ordered rest and a prolonged holiday from his work. I saw him again a few months later. His signs were as before. He reported himself as distinctly better. I ventured to display a little optimism, but did not sanction a resumption of duties. Two days later he was sitting still reading a book when he fell back dead.

The presence of any physical sign of organic cardiac change in association with angina calls for a guarded verdict.

Status Anginosus

Of the 'allied seizures', the first to be discussed is the condition usually called 'status anginosus', in which the sternal or praecordial pain continues with great intensity, or is repeated again and again at short intervals; in which nitrites fail to bring relief, and even heavy doses of morphine may be only partially successful. This terrible condition is now shown to be caused in almost every case by coronary thrombosis with local ischaemia of the heart-muscle. With it there may be slight fever for a few days and a transient leucocytosis. The pain is sometimes referred to the epigastrium, and, with the associated grey pallor and collapse, may be so strikingly suggestive of a perforated ulcer as to lead to operation. Within a few hours or days symptoms of heart failure may supervene with congestive signs; the blood-pressure falls; the heart-sounds become distant and faint; occasionally a fleeting pericardial rub is heard. The patient may die within minutes, hours, or days of the first onset, or he may recover with a crippled, or a healed and apparently healthy heart. Some patients are able to return to their normal occupations. An electrocardiogram usually reveals evidence of the myocardial damage. While in some cases the gravity and long continuance of the pain are terrible to witness, in others the gravity of the attack is less apparent, or in the place of continuous pain there may be brief recurring anginal attacks at rest. Several patients, giving a typical history of an attack, have been referred to me as cases of 'bad indigestion'. In these physical signs may be inconspicuous or lacking, but the electrocardiogram may bear witness to the presence of muscle damage. After the acute phase patients may be troubled with neuralgic pains in the back of the neck and occiput. On returning to active life the angina of effort or dyspnoea may be noted for the first time.

Perusing the clinical accounts of cases of angina pectoris by such great masters as Latham, Osler, Clifford Allbutt, and Mackenzie we are now able to pick out with some confidence, *from their descriptions alone*, examples of angina which must have been due to coronary occlusion. Turning

to our old case-notes, we also find descriptions which enable us to separate this variety from the general group of anginas. Out of curiosity I have recently looked up the accounts of John Hunter's illnesses;[1] from these it is clear that his first anginal seizure was in all probability due to a coronary thrombosis, and at necropsy 20 years later typical scars were found in his heart. *Any prolonged anginal attack should suggest the possibility of a coronary thrombosis.*

Anaemic Angina

Severe anaemias may cause angina of effort and can be completely relieved by successful treatment of the anaemia.

Case 6. A successful business man, aged 50, had lost something of his customary fitness after a period of stress and worry, and then had all his teeth extracted. Shortly afterwards he developed attacks of angina pectoris, especially when walking after meals. It then became apparent that he was losing weight and colour. Vomiting was an additional symptom. I noted him as of broad build and short-chested. He was very obviously anaemic. His tongue was sore. Heart not enlarged. A soft systolic murmur. B.-P. 120/85. His haemoglobin was 30 per cent. and his blood-picture typical of pernicious anaemia. He was treated with liver extract. In the next 8 months his weight rose from 10 st. 6 lb. to 12 st. 0 lb., and he lost all his general symptoms; he no longer experienced anginal pain, and again led an active life.

Vasovagal Attacks

There is a type of vasomotor storm, beautifully described by Gowers in his 'Borderland of Epilepsy' under the heading of *vasovagal attacks*, which may cause confusion and lead to a diagnosis of angina. In my own experience these seizures have always occurred in the victims of anxiety, usually combined with slight general physical ill-health; they have been rather more common in women. The leading symptom is not pain, but 'the sense of dying'. The attacks are not as a rule related to physical effort. Pain may be altogether absent, or where present amounts to a sense of constriction with a curiously frequent mention of a 'tugging, pain up the left side of the neck'. Other vasomotor pheno-

[1] See Lecture XXV.

mena are present, and curious sensations are referred to other viscera. The pulse may be quick or very slow in the attacks, which last minutes or an hour or more, and are followed by feelings of prostration. To the best of my knowledge these seizures, however alarming, never kill.

Abdominal Angina

What else may we include within the category of 'allied seizures'? Firstly, there is abdominal angina in which (as distinct from the epigastric form of angina pectoris) the pain is felt at or below the umbilical level.

Case 7. An ex-sailor, aged 50, with syphilitic aortitis and aortic regurgitation, complained of 'terrific' pain felt just below the navel, coming always as the result of effort, and usually of very slight effort, such as getting out of bed or even turning over in bed. There was tenderness along the course of the abdominal aorta, but no sign of aneurysm.

Amyl nitrite may bring relief in these cases.

We may also meet with benign abdominal angina.

Case 8. A woman was sent to my Out-Patients as a gastric case. On inquiry her symptom was found to be a central abdominal pain induced by walking and eased when she sat down. She had a throbbing abdominal aorta and definite, though slight, signs of hyperthyroidism, and was clearly a nervous subject.

'Status anginosus abdominis' also occurs, and may lead to a diagnosis of acute abdominal disease.

Case 9. Recently I performed a necropsy on a woman who died as the result of an attack of what might well be thus designated. She had been admitted to a surgical ward as an acute abdominal emergency, collapsed and pale, and in great pain. An exploratory laparotomy failed to reveal any perforated viscus or adequate cause for her symptoms. She did not long survive. Before starting the necropsy I discussed the possibility of coronary thrombosis. We found advanced syphilitic disease of the abdominal aorta, and the coeliac axis and right renal artery were plugged with recent thrombus.

Angina Cruris

Angina may also occur in the leg. I prefer the title of 'angina cruris' to 'intermittent claudication (or limping)', which is the term usually employed to describe a severe type

of painful seizure affecting the leg in patients with arterial disease. This pain is characteristically induced by walking and relieved on standing still. Occasionally, however, the pains, like those of angina pectoris, may develop at rest, and they may even be accompanied by angor animi. Furthermore, angina pectoris and angina cruris are not infrequently recorded in the same patient.

Case 10. An elderly male had long had pain on walking. On one occasion he was seized with violent pain in the leg while sitting at his fireside. He was carried to bed and passed a night of physical and mental anguish. With evident awe he described a feeling during the attack 'as though his number was up'.

Benign cases of angina cruris with recovery have also been recorded. With actual arterial occlusion, as in old age and in thrombo-angiitis obliterans, there may arrive a 'status anginosus cruris', with more persistent and intolerable pain and pallor and coldness or gangrene of the toes or foot.

Thus we have, alike in the pectoral and the peripheral anginas, benign types of functional disorder due presumably to neuro-muscular errors of arterial adaptation; graver types with disease and loss of resilience in the arterial wall; and those gravest types of all in which there is actual vascular occlusion with secondary ischaemic consequences.

I have laid some stress upon the peripheral forms of angina, for the analogies are close, and I cannot but think that they help to illuminate the pectoral form, to explain some of its symptoms, and to establish it as expressive of vascular disorder or disease rather than of any primary cardiac affection.

The Physiology of Anginal Pain

The cause of anginal pain has been a matter for philosophic debate amongst physicians in many generations. Clinical observation and experiment have now established that ischaemia of the heart-muscle (as of the leg-muscles in intermittent claudication) is the essential factor, probably (as Lewis has suggested) with accumulation of chemical metabolites in the affected muscle-fibres.

Could this conclusion have been reached by clinical and

pathological observation and deduction alone? If we review all the conditions in which angina pectoris is a symptom and seek to isolate a common factor, we can at least claim to arrive very near the mark.

In its worst and most sustained form angina pectoris accompanies actual occlusion of a coronary vessel. In its next gravest form it accompanies coronary arteriosclerosis without occlusion, but here narrowing of the vessel wall or inability on the part of the vessel to dilate and convey an adequate tide of blood to the muscle may be presumed to operate. In 'nervous' and 'tobacco' angina and in vasovagal attacks arterial spasm is a reasonable hypothesis. In vasovagal attacks I have witnessed palpable alterations in the radial artery and remarkable fluctuations of blood-pressure. In aortic incompetence, when due to syphilis, the mouths of the coronary arteries may be encroached upon, and both in the rheumatic and syphilitic types the intra-aortic pressure of blood may not be sufficiently sustained to flush the coronary circulation adequately at times of stress. In hyperthyroidism and simple paroxysmal tachycardia, in both of which conditions I have noted angina as an occasional symptom, the heart (although we believe the vessels to be normal) is working 'overtime', and the circulation, as in the violent efforts of health, cannot quite keep pace. Finally, we are left with the angina which may be symptomatic both of pernicious and of other types of anaemia, and which can occur in cases lacking all evidence of cardiac or arterial disease and all the other factors mentioned above, excepting only the poverty of the blood-supply to the heart relative to the demands put upon it during a phase of increased work. We are thus left with cardiac anaemia or ischaemia as the common factor.

Prognosis

Prognosis, always a most difficult branch of our art, must depend to some extent upon the group to which we relegate our case. In the nervous and anaemic types of angina pectoris, in some of the mild post-infective types, and, perhaps, in some associated with transient or developing high blood-pressure, the outlook as regards life and return to health

may be quite good. In the middle-aged type with arterial disease it must always be guarded, and the more so if there is any clinical or electrocardiographic evidence of structural change in the heart. In the absence of such evidence, and if a suitable mode of life can be enjoined, the outlook need not of necessity be gloomy. In the third group with coronary occlusion the prognosis is often obviously and immediately very bad, or even if recovery from the acute phase follows, life is shortened. It is established, however, that recoveries and even a return to a normal way of life may follow the plugging of a smaller branch and even some of the graver varieties of status anginosus which entitle us to presume a considerable myocardial infarct.

The prognosis in the peripheral forms of 'angina' must also depend on the presence or absence of organic change in the arteries affected, and is obviously gravest when arterial thrombosis has occurred.

XXV

A NOTE ON JOHN HUNTER'S CARDIAC INFARCT[1]

THE past ten years have witnessed a steadily growing output of literature relating to coronary thrombosis and cardiac infarction. Extensive surveys of clinical and pathological material, together with cardiological studies, have established and defined the syndrome which characterizes this grave vascular accident, and indicated its relationships with angina pectoris. We now know that the status anginosus generally proclaims a coronary occlusion, and that, notwithstanding the gravity of the event and its high immediate mortality, survival is common, and a return to a life of modified or even full activity not impossible. From the descriptions of anginal cases left to us by the great masters, including Latham, Osler, Clifford Allbutt, and Mackenzie, it is possible to select indubitable earlier examples of seizures due to this cause. It is noteworthy that Heberden himself mentioned a few cases in which the pain persisted for hours or days.

Recollecting the minuteness of the clinical detail in Sir Everard Home's account of Hunter's illnesses, it occurred to me to re-examine the narrative of these, and particularly the descriptions of his alarming vascular crises. The story of Hunter's angina, of his foreboding that his death might be precipitated by any one who should anger him, and of his actual demise in such a circumstance, is common property, and has found its place in the text-books and been recounted to generations of students. Edward Jenner was alive to the significance of Hunter's symptoms but kept the information from his friend. It is not, I believe, so widely recognized that his very first seizure was, in all probability, due to a coronary thrombosis; that he survived it for 20 years; and that, on examination after death, two fibrotic scars were found in the wall of his heart.

The descriptions which follow are drawn from Joseph

[1] *Lancet*, 1928, i. 339.

Adams's *Memoirs of the Life and Doctrines of the late John Hunter, Esq.* (London, 1817), in which the author includes full quotations from Sir Everard Home's *Life*. Sir Everard Home's account was based on observations of his symptoms noted by Hunter himself at the time of their occurrence, or dictated to Sir Everard Home when he was too ill to write. I have italicized some of the more apposite passages.

'In the spring of 1760, in his forty-first year, he had a regular fit of the gout, which returned the three following springs, but not in the fourth; and in the spring of 1773, having met with something which very forcibly affected his mind, he was attacked, at ten o'clock in the forenoon, with a pain in the stomach, about the pylorus; it was the sensation peculiar to those parts, and became so violent, that he tried change of position to procure ease; he sat down, then walked, laid himself down on the carpet, then upon chairs, but could find no relief. He took a spoonful of tincture of rhubarb with 30 drops of laudanum, without the smallest benefit. While he was walking about the room, he cast his eyes on the looking-glass, and observed his countenance to be pale, his lips white, giving the appearance of a dead man: this alarmed him, and led him to feel for his pulse; but he found none in either arm. He now thought his complaint serious. Several physicians of his acquaintance were then sent for: Dr. William Hunter, Sir George Baker, Dr. Huck Saunders, and Sir William Fordyce, all came, but could find no pulse; the pain still continued, and he found himself at times not breathing. Being afraid of death soon taking place if he did not breathe, he produced the voluntary act of breathing, by working his lungs by the power of the will; the sensitive principle, with all its effects on the machine, not being in the least affected by the complaint. In this state he continued for three-quarters of an hour, in which time frequent attempts were made to feel the pulse, but in vain; however, at last, the pain lessened, and the pulse returned, although at first but faintly, and the involuntary breathing began to take place. While in this state, he took Madeira, brandy, ginger, &c., but did not believe them of any service, as the return of health was very gradual; in two hours he was perfectly recovered.'

Hunter was aged 45 at the time. The restlessness which he showed in the attack is now known, in contradistinction to the strict immobility of ordinary angina, to be a not uncommon feature of coronary thrombosis. The reference of pain to the epigastrium is also a recognized feature, and may sometimes lead to a faulty diagnosis of acute abdominal disease. *Writing a hundred years ago Joseph Adams was*

sage enough to argue, and in opposition to Hunter's own idea, that, although the pain was apparently in the stomach, the actual seat of it was in the heart.

'That the disease was in the heart can now admit of no doubt: the cessation of the pulse is what might be expected from violent inflammation, as will be hereafter explained; *but the strongest proof that the heart at that time suffered* an *alteration in its structure, the effect of inflammation, is, that for the remainder of his life the patient suffered all the effects of* angina *pectoris*. . . .'

In 1776 Hunter had a serious illness in which vertigo and sickness played a prominent part. In 1785 he had another serious illness.

'About the beginning of April 1785 (Sir Everard Home informs us), he was attacked with a spasmodic complaint, which at first was slight, but became afterwards very violent, and terminated in a fit of the gout in the ball of the great toe; this, like his other attacks, was brought on by anxiety of mind. The first symptom was a sensation of the muscles of the nose being in action; but whether they really were, or not, he was never able to determine. This sensation returned at intervals for about a fortnight, attended with an unpleasant sensation in the left side of the face, lower jaw, and throat, which seemed to extend into the head on that side, and down the left arm, as low as the ball of the thumb, where it terminated all at once: these sensations were not constant, but returned at irregular times; they became soon more violent, attacking the head, face, and both sides of the lower jaw, giving the idea that the face was swelled, particularly the cheeks, and sometimes slightly affected the right arm. After they had continued for a fortnight, they extended to the sternum, producing the same disagreeable sensations there, and giving the feel of the sternum being drawn backwards towards the spine, as well as that of oppression in breathing, although the action of breathing was attended with no real difficulty: at these times the heart seemed to miss a stroke; and upon feeling the pulse, the artery was very much contracted, often hardly to be felt, and every now and then the pulse was entirely stopt. He was afterwards attacked with a pain in the back, about that part where the œsophagus passes through the diaphragm, the sensation being that of something scalding hot passing *down the œsophagus. He was next seized with a pain in the region* of the heart itself; and last of all, with a sensation in the left side, nearly in the seat of the great end of the stomach, attended with considerable eructations of wind from that viscus: these seemed to be rather spasmodic than a simple discharge of wind, a kind of mixture of hiccough and eructation, which last symptoms did not accompany the former, but came on by themselves. In every attack there

was a raw sore feel, as if the fauces were excoriated. All these succeeding symptoms (those in the stomach and nose only excepted) were in addition to the first, for every attack began with the first symptoms. The complaint appeared to be in the vascular system, for the larger arteries were sensibly contracted, and sore to the touch, as far as they could be touched, principally in the left arm; the urine at those times was in general very pale.

'*These symptoms increased in violence at every return, and the attack which was the most violent came on one morning about the end of April, and lasted about two hours. It began as the others had done, but having continued about an hour, the pain became excruciating at the apex of the heart; the throat was so sore as not to allow of an attempt to swallow any thing, and the left arm could not bear to be touched, the least pressure upon it giving pain; the sensation at the apex of the heart was that of burning or scorching, which, by its violence, quite exhausted him, and he sunk into a swoon or doze, which lasted about ten minutes, after which he started up, without the least recollection of what had passed, or of his preceding illness. I was with him during the whole of this attack, and never saw any thing equal to the agonies he suffered; and when he fainted away, I thought him dead, as the pain did not seem to abate, but to carry him off, having first previously exhausted him.*

'He then fell asleep for half an hour, and awoke with a confusion in his head, and a faint recollection of something like a delirium; this went off in a few days.

'The affections above described were, in the beginning, readily brought on by exercise; and he even conceived, that if he had continued at rest, they would not have come on: but they at last seized him when lying in bed, and in his sleep, so as to awaken him. Affections of the mind also brought them on; but coolly thinking or reasoning did not appear to have that effect. While these complaints were upon him, his face was pale, and had a contracted appearance, making him look thinner than ordinary; and after they went off, his colour returned, and his face recovered its natural appearance.'

This description clearly refers to a further series of vascular storms of a critical kind. May they possibly have accompanied a second coronary thrombosis? This illness laid him low from the beginning of April until the latter part of May, and ended with an attack of gout. After it he remained more than ever subject to the angina of effort or emotion.

In 1789 he suffered a loss of memory and more vertigo. Between 1791 and 1793 his anginal attacks became increasingly frequent and more prolonged, and arrived for lesser causes.

'On the 16th of October 1793, when in his usual state of health,

he went to St. George's Hospital, and meeting with some things which irritated his mind, and not being perfectly master of the circumstances, he withheld his sentiments; in which state of restraint he went into the next room, and turning round to Dr. Robinson, one of the physicians of the hospital, he gave a deep groan, and dropt down dead!'

The body was examined after death, and the findings in regard to the heart were reported as follows:

'The pericardium was very unusually thickened, which did not allow it to collapse upon being opened; the quantity of water contained in it was scarcely more than is frequently met with, although it might probably exceed that which occurs in the most healthy state of these parts. The heart itself was very small, appearing too little for the cavity in which it lay, and did not give the idea of its being the effect of an unusual degree of contraction, but more of its having shrunk in its size. *Upon the under surface of the left auricle and ventricle, there were two spaces nearly an inch and half square, which were of a white colour, with an opaque appearance, and entirely distinct from the general surface of the heart: these two spaces were covered by an exudation of coagulating lymph, which at some former period had been the result of inflammation there.* The muscular structure of the heart was paler and looser in its texture than the other muscles in the body. There were no coagula in any of its cavities. The coronary arteries had their branches which ramify through the substance of the heart in the state of bony tubes, which were with difficulty divided by the knife, and their transverse sections did not collapse, but remained open. . . . The semilunar valves of the aorta had lost their natural pliancy, the previous stage to becoming bone, and in several spots there were evident ossifications. The aorta, immediately beyond the semilunar valves, had its cavity larger than usual, putting on the appearance of an incipient aneurism: this unusual dilatation extended for some way along the ascending aorta, but did not reach so far as the common trunk of the axillary and carotid artery. The increase of capacity of the artery might be about one-third of its natural area; and the internal membrane of this part had lost entirely the natural polish, and was studded over with opaque white spots, raised higher than the general surface. . . .'

To this account Joseph Adams added the following commentary:

'The opake spot in the heart was probably formed during the severe illness of 1773, at which time the heart refused to act, the invariable consequence of high inflammation in a muscular part. Such is the immediate effect during the severe paroxysm of inflammation in the heart. The consequences for the remainder of life must depend on

the alteration, if any, which had taken place from the inflammation. Sometimes the heart never recovers, and the circulation is carried on feebly till the patient expires, without any external cause: sometimes the heart is dilated by the afflux of blood on which it is at first unable to contract, and after a time contracts with irregularity, from an incapacity to acquire its original form. In Mr. Hunter's case, from an alteration in its texture, its actions became irregular; and consequently the action of the lungs. This constitutes angina pectoris, with which, Sir Everard Home informs us, Mr. Hunter was afflicted for the last 20 years of his life, the exact period of this illness.'

If it be accepted—and it is difficult to offer any alternative explanation—that Hunter's first seizure was due to a cardiac infarction, it is surely a most remarkable feature of his case that he should not only have survived it for 20 years, but that for the greater part of that time he should have been able to devote himself to labours which continued to add lustre to his earlier fame. This chapter of Hunter's life which is concerned with his illnesses affords us a glimpse of the great strength of will and the scientific interest with which he constantly met them, and only serves to increase our admiration of the man. I do not know whether any parallel case can be quoted, but for the benefit of the physician faced with the delicate task of prognosis in this grave and disturbing malady it is at least gratifying to record that it may sometimes be consistent with long years of useful activity.

XXVI

THREE CASES OF CARDIAC DISTRESS[1]

THE heart, embarrassed by disease, complains in various ways. The symptoms by which we recognize its complaint may be referred to the organ itself, as in the case of pain or palpitation, or to other organs and tissues whose circulation is impaired in consequence of the cardiac disability. Thus, you are all familiar with dyspnœa, œdema, cyanosis, and engorgement of the liver as manifestations of heart failure.

The three cases from Clinical Ward which I bring before you to-day are undoubted examples of cardiac or cardiovascular disease with distress or failure, but the pictures presented by them are so different that you would at once surmise, and rightly, that each must express a different pathology. Each case holds for us lessons in respect of diagnosis, prognosis, and treatment which I shall endeavour to unfold to you in considering their several histories.

The first is that of a married woman aged 43, who was admitted to Miriam Ward in April 1928. She had rheumatic fever at the age of 21, and has nine children alive and well; two others died in infancy. In the autumn of 1927 we obtain the first clear account of cardiac distress, for she was admitted to the Rotherhithe Infirmary for dyspnœa and pain in the left chest, and remained there for a month. Since then she has rested at home, but, becoming less well latterly with cough, pain round the waist, dyspnœa on effort, and, finally, a sharp pain on breathing in the left chest, she was sent up to Guy's. Her pulse on admission was found to be rapid and irregular, the excursions at the wrist were of varying size and some pulsations failed to reach the wrist. We were of the opinion that she had auricular fibrillation, but at the same time noted frequent short paroxysmal phases in which the rhythm appeared to be regular. This was of interest, as Dr. Campbell's first electrocardiogram showed

[1] *Guy's Hosp. Gazette*, 1928, xlii. 502.

the presence of auricular flutter, although under treatment with digitalis this was quickly replaced by fibrillation. Fibrillation as a late consequence of rheumatic fever is almost always an association of mitral stenosis, and we thought we had good support for a diagnosis of mitral stenosis in the remarkably deep red colour of her lips, which you can see for yourselves to-day, and which the patient assures us is not due to the use of a lipstick. The heart was enlarged and there was a systolic murmur at the apex, but at first we could determine no confirmatory pre-systolic thrill or rumbling murmur. Other findings included considerable enlargement of the liver, albuminuria, and a dry localized pleuritic friction at the left base to account for her pain. This, we thought, might be due to a small pulmonary infarction, and held as further evidence in favour of mitral stenosis. Improvement rapidly followed rest in bed and digitalization. The liver margin has retired, the albumin has disappeared, the urinary output has increased, the pulse-rate has fallen, and you can now feel and hear for yourselves a thrill and a diastolic murmur. Her full diagnosis might therefore be stated briefly as follows: 'Rheumatic carditis. Mitral stenosis. Auricular flutter, giving place to fibrillation. Hepatic and renal engorgement. Pulmonary infarction.' I should like to impress upon you that a large part of this information could be gleaned from a glance at her lips and a finger on her pulse after listening to the account of her symptoms, and that first impressions, often valuable but never wholly to be trusted, were in this case fully borne out by the subsequent findings. How is it that she was able to support eleven pregnancies without mishap? We are commonly taught that mitral stenosis must in many cases be regarded as a contra-indication to future pregnancies because of the added strain and risk which these entail. I think it is reasonable to conclude from the history of this case that, although mitral stenosis has been present for years, the faulty rhythm and muscle failure are of much more recent origin.

The case exemplifies well the rapid improvement which may take place with rest and digitalis. It is now important that she should curtail her domestic activities, and with a

growing family this can fortunately be nrranged. It is nlso important that she should continue to take a snnall dose of digitnlis indefinitely. So often I find that the drug has been discontinued when n certain point of improvement has been reached. I know no contra-indication in tolernnt patients to the tnking of small doses over very long periods, nnd 15 to 20 minims of the tincture daily may well help to protect this patient against recurrences of her recent illness.

This type of case will be famdiar to you all. The other two are more dramatic and less common, but you should be nequainted with the clinical pictures which they present.

Mr. H—— N——, nged 55, a porter, was admitted to John Ward for collapse nnd extreme dyspnoea. At the nge of 9 he had extensive syphilitic ulceration of the right arm, of which he bears the scnrs. We have no knowledge of how the disease was acquired. Two and n half yenrs ago he was taken to hospitnl for nn nttack similar to that for which he was recently ndmitted. Before that he had had slighter nttneks, but it is noteworthy that he has since remained at work until the very day of his admission. He was admitted in the early hours of the morning of 27 April, having been found in a collnpsed condition in the street. His colour was a greyish-blue; his skin was cold and covered with sweat; he had no pain, but breathing was laboured and 'accompanied by a continuous bubbling sound'; froth was trickling from the corner of his mouth; the pulse was irregulnr, and its rate 140 to the minute; respirations 36 to the minute; the apex beat was in the fifth space, 1½ inches outside the nipple line; praecordial dullness extended to the right of the sternum. The liver mnrgin wns tender. He was given nasal oxygen, nad nne-hundredth of a grain each, hypodermically, of atropine and strophanthin, and 8 ounces of blood were withdrawn from his median basilic vein. From looking and feeling desperately ill, his appenrnnce and sensations steadily improved, so that when I first saw him about 12 hours later he was quite comfortable and the bubbling in his lungs had nll subsided. As you see, he is now free from all embarrassment, but by his Corrigan's pulse and nortic murmurs you can recognize a part of the underlying

trouble. The history is that of the condition known as acute pulmonary oedema. Pulmonary oedema akin to this may result from inhalation of irritant gases such as phosgene gas, first used as a lethal weapon in the 1914–18 war, and may very rarely be symptomatic of an acute pulmonary infection. But the cases encountered in practice are usually a consequence of cardio-arterial disease, and the oedema is thought to be a result of serous transudation from the smaller pulmonary vessels in conditions in which the left ventricle finds itself unable to transmit the whole output of the right ventricle—in fact of acute left ventricular failure. In support of this hypothesis we see acute pulmonary oedema, principally in cases of arterial and renal disease with high blood-pressure and in aortic incompetence, conditions in which the left ventricle is overtaxed. This man has a to-and-fro murmur in the aortic area which we believe to be due to syphilitic aortitis—his Wassermann reaction is strongly positive, and you will remember his early history; in addition, his blood-pressure has been recorded as high as 185 systolic, 100 diastolic. The characteristic features of acute pulmonary oedema are sudden onset, rapid development of dyspnoea and distress with moist sounds all over the chest, and the outpouring, sometimes in enormous quantities, of a white or slightly blood-stained frothy fluid, resembling the spume on the lips of an over-driven horse. The treatment in grave cases should include continuous intranasal oxygen, a hypodermic injection of morphine with atropine, and venesection. From lesser attacks the patient may recover spontaneously; from seemingly hopeless attacks, in which drowning seems imminent, he may be dramatically reclaimed by timely aid to survive for longer or shorter periods. As the underlying cause is generally some serious organic change in the heart and arteries, the ultimate prognosis can seldom be good.

Our third case is that of a man aged 54. He has consumed too much alcohol in the past, and was once in Guy's for a fractured leg; otherwise his medical history was uneventful until six months ago. He then began to notice a sense of retrosternal discomfort on mounting stairs or with other exertion. At times there was actual pain, but this always

disappenred immediately with rest. On the morning of 19 April he wns suddenly seized at his place of business with n violent retrosternal pain. He had to lie down, but could not remain still, nnd rolled nbout in the extremity of his agony. He was brought to the surgery in a state of collnpse with n rnpid, feeble pulse. Amyl nitrite gave instant but incomplete relief. He went home, but had a return of pain and was ndmitted the next day. He was noted ns nervous, shaky, and plethoric. His pain was still located behind the middle of the sternum. His pulse was 98 to the minute nnd regular. His blood-pressure, which had been 160 systolic in the surgery on the previous day, hnd fallen to 140. The next day it was 120 and the next day 90—a very low figure for n man of his build—nt which it has since remained. The impulse was neither visible nor palpable; the left border by percussion was 4 Inches from the midline. The most striking physicnl sign, and this has persisted, as you shall hear for yourselves, was the inaudibility of the heart-sounds. With very careful nttention they can now just be heard, faint and far nway nnd equnlized. There is no considerable emphysema or other intervening cause to explain this, and we believe it to be due to a serious myocardial damage. For mnny days after ndmission the chart shows pyrexia, gradually settling by lysis. There was a leucocytosis nt first of 29,000 cells per c.mm., which, in concert with the declining temperature, has gradually fallen to 11,500. The history of onset nnd the symptoms and signs which I have described are characteristic of coronary thrombosis with cardiac infarction. Of this condition there are nt least twelve importnnt manifestations, including:

(1) Onset with status anginosus, or rapidly repeated anginal seizures at rest, nlthough it is believed that coronary occlusion without pain can also occur.
(2) Restlessness in the attack, instead of the usunl immobility of angina pectoris.
(3) Failure of nmyl nitrite, and relief with difficulty even by morphine, large or frequent doses often being necessary.
(4) Shock-like symptoms in the graver cases.

(5) Epigastric instead of sternal pain, with simulation of an acute abdominal catastrophe in some cases.
(6) Fever following the attack, transient or lasting for several days.
(7) Pericardial friction, usually very transient.
(8) A falling blood-pressure.
(9) Development of signs and symptoms of congestive failure in the graver cases.
(10) Faintness and equalization of the heart-sounds and sometimes arrhythmia.
(11) Leucocytosis.
(12) Certain electrocardiographic changes indicative of myocardial damage.

Of these twelve manifestations, no less than eight, including the electrocardiographic changes—which Dr. Maurice Campbell reports as typical—were recorded in the case of this man. What are we to presume is the associated morbid change? We can with some confidence assert, with our growing knowledge of the syndrome, that he has a branch of a coronary artery occluded by a thrombus, the thrombus being secondary to coronary atheroma, and that he has ischaemia with necrosis of a part of his ventricular wall. Although he is now comfortable, the prognosis in this case is not good, and clearly when a large branch is blocked the ultimate outlook is always bad. But I believe it to be wrong to take a gloomy view in every case of coronary thrombosis. I have notes of patients who led active lives for upwards of ten years. John Hunter lived and worked for twenty years after his. In the initial stage treatment must include absolute rest in bed for an adequate period, the duration being never less than several weeks and regulated by the severity of the initial symptoms, the progress of the case, and other evidences. For the pain morphine should be given. Small doses of digitalis are thought to be desirable if there is tachycardia or arrhythmia.

I have shown you our three cases of cardiac distress. The first was admitted for pleuritic pain and dyspnoea on effort; the second for sudden and urgent dyspnoea and obvious

oedema of the lungs; the third for intense and sustained retrosternal pain, followed by pyrexia, a falling blood-pressure, and an inaudibility of the heart-sounds so striking that I have brought him here principally for you to observe this sign for yourselves. With some confidence we have been able to attach a causal pathology in each instance. Incidentally, too, these cases have served to illustrate some of the effects of the three commonest causes of organic cardiac disease, namely, rheumatic fever, syphilis, and arteriosclerosis.

XXVII

THROMBOPHLEBITIS MIGRANS[1]

THE occurrence of cases of phlebitis with thrombosis, sometimes widespread and recurrent but lacking any clear aetiological associations, has long been recognized. Such cases, although not common, are by no means excessively rare. They are distinct both in their history and in their course from those forms of thrombophlebitis which complicate the specific fevers or follow operations and the puerperium, or which have been recorded in connexion with syphilis, tuberculosis, malignant disease, and anaemia. They are not due to varicosity or other chronic disease of the veins. It is possible that some of the cases of phlebitis formerly ascribed to gout may have belonged to this special group. Sir James Paget [1] reported cases of diffuse superficial phlebitis, both gouty and non-gouty, as long ago as 1866. More recently an interesting account of 4 cases has been given by Moorhead and Abrahamson [2], under the title of 'Thrombo-phlebitis Migrans', in three of which wandering superficial thromboses of this kind were accompanied by visceral thromboses. Five[2] similar cases, 4 of them with visceral thromboses, have come my way, and I am sure it will be in the experience of others to have encountered examples of this condition from time to time in the ordinary course of practice. Campbell and Morgan [3] have lately recorded a case of brachial thrombophlebitis complicated by severe headache and tubular vision, due possibly to thrombosis of posterior cerebral vessels, and also by cardiac symptoms with cardiographic findings suggesting a coronary thrombosis. Carey Coombs [4] has mentioned cases of coronary thrombosis in association with peripheral

[1] Based on a communication given before the Association of Physicians in London on 6 June 1930 (*Lancet*, 1930, ii. 731).

[2] My experience has since been increased by 15 additional cases, and I have now seen migratory phlebitis antecedent once to the discovery of deep-seated malignancy and once to bacterial endocarditis; I have also seen it in a gouty subject.

phlebitis, including one case in which a pulmonary and then a cardiac thrombosis preceded thrombophlebitis in the thigh. Briggs [5] and Herrick [6] have reviewed the subject of wandering phlebitis, but they gave no account of visceral lesions.

The name thrombophlebitis *migrans* seems to me admirably suited to the condition. The process is essentially migratory, the lesions showing dissemination both in space and time, as will be seen from an examination of the case reports given hereunder. The same nomenclature has been applied to a rarer condition in which the phlebitis spreads gradually along the course of a particular vein or veins. As, however, this may be described more correctly as a 'creeping' than a 'wandering' process, it would seem that thrombophlebitis migrans is more appropriate to the disease under discussion.

Moorhead and Abrahamson expressed themselves as unable to throw any light on the aetiology of the condition. In one of their cases, it is true, the first superficial phlebitis followed a mosquito bite on the same limb after an interval of a week; a month previously, however, the patient had had an unexplained pleurisy which, in the light of later events, may well have been due to a primary pulmonary thrombophlebitis. In another case the first phlebitis occurred in the leg three months after a superficial burn on the corresponding foot. In a third there was severe pyorrhoea. Owen [7, 8] has sought to associate the condition with influenzal epidemics, but in none of my cases nor in those described by Moorhead and Abrahamson was there any good reason to suspect influenza as an aetiological factor. I am, however, inclined to agree with him when he suggests that many of the obscure pleurisies of practice associated with red haemoptysis are due to small pulmonary thromboses of infective origin. The association in one of my cases with a subsequent bacterial endocarditis (*Strep. viridans*) and the not infrequent association (described hereunder) with dental sepsis lead me to suggest that—where gout can be excluded—a phlebitis starting in one of the valves of a vein and consequent upon a transitory bacteri-

aemia with *Strep. viridans* may prove to be the usual pathology of this condition.

The cases which I propose to describe confirm and amplify the observations of Moorhead and Abrahamson, and also serve to indicate some of the difficulties in diagnosis which may arise over the visceral lesions. One case is included in which there were symptoms of visceral thromboses without the involvement of any superficial vein. In 3 of the 5 cases there was good reason to suspect the influence of chronic focal sepsis. The period within which symptoms of wandering thrombophlebitis continued to arrive is indicated in brackets at the heading of each case.

Reports of Five Cases

Case 1. *Thrombophlebitis affecting both legs* (1924–7).—A young man, aged 23, previously in robust health, first developed phlebitis in the calf of the right leg in 1924. This was slow to mend, and he eventually had the vein excised. He was then well until the first week of October 1927, when he again developed phlebitis in both legs. A fortnight later he was found to have a tender molar tooth. This was extracted. When I first saw him in consultation with Dr. C. Sherris on 27 November 1927, the legs had cleared completely, but he had just developed a fresh phlebitis involving a short segment of one of the veins on the dorsum of his right foot. At one time he had had an enlarged epitrochlear gland, but there was no history of syphilis, and the Wassermann reaction was negative. There was *no gouty history. A differential blood count showed no abnormality.* Clotting time was normal. Mr. Kelsey Fry, on clinical and radiographic evidence, advised the extraction of four dead teeth, and reported as follows: 'Three of the dead teeth that I have extracted showed marked apical absorption, and as they had never been filled, I must presume the infection was blood-borne. Were they the cause of the thrombosis, or are they due to the same cause?' Two years and a half have now elapsed without any further symptoms of phlebitis or other ill health.

Case 2. *Thrombophlebitis affecting one leg, both lungs, and intra-abdominal veins* (March–July 1924).—A man, aged 58, was submitted to my care by Dr. T. D. H. Holmes for phlebitis of the right leg, which had already necessitated his lying up for a month.

For some months previously he had felt 'out of sorts' and disinclined for work, but he had had no other illness of importance. For ten days prior to my first seeing him he had had an almost continuous stomach-ache, but in the last two days both this and the leg dis-

ficial, and there was no evidence of extension to larger or deeper vessels. The temperature did not exceed 100° F. I diagnosed pulmonary thrombophlebitis.

On the next day he started to have some small haemoptyses and simultaneously developed a fresh phlebitis on the dorsum of his right foot. Excepting for transient pains in the left axilla and the left loin he had no further symptoms suggestive of visceral involvement, but progress to complete recovery was interrupted by five other very small thromboses affecting superficial veins of the left leg and foot. During the earlier phase of the illness a blood culture was negative; the leucocyte count was 12,200 cells per c.mm., whereas he had always previously shown a marked leucopenia; a *Streptococcus viridans* was grown from the sputum. Radiograms later showed marked opacity of the right antrum, a doubtful right frontal sinus, and three definitely infected teeth. The infected teeth were extracted. The last thrombosis followed a few weeks after the extractions.

It seemed reasonable to suppose that this wandering thrombophlebitis was a late sequel of his septic illness of the previous year, and due to lingering focal infection. There was no reason to consider gout as a factor.

Case 4. *Thrombophlebitis affecting both legs, both lungs, and a cerebral vein* (1924–9).—On 13 April 1929 I was asked to see, in consultation with Dr. G. T. Cregan, a spinster, aged 53, who gave the following history.

In 1897 she had rheumatic pericarditis. In 1907 she had herpes of the scalp and developed anginal attacks, for which she saw Sir James Mackenzie. During the war period, in which she was employed with arduous and responsible duties, she became unfit for a time, and a streptococcus was grown from the urine in 1915 and again in 1917. In 1919 she had a return of anginal pain and severe streptococcal infections of the throat. Between 1919 and 1924 she was treated with vaccines. In 1924 she had an acute illness with anginal symptoms, rigor, a pulse-rate of 140, thrombosis in the left leg, and bilateral pulmonary 'embolisms' with haemoptysis. In January 1925 she had otitis media. In May 1928 she had a septic throat and right-sided 'pleurisy', and coughed up a little blood. In September 1928 she felt stiff in her left face, her left hand became 'woolly', and she was sick. She was at this time in bed for a month with slight fever. By November 1928 she was again very ill with haemoptysis, and some sterile fluid was aspirated from the right chest. Her sputum grew Friedländer's bacillus, streptococci, and pneumococci. In December 1928 she had a new thrombosis in the left leg with oedema. In January 1929 the right leg became affected, with red patches and a tender point in the groin.

The patient was of obese habit, and at the time of my examination both legs remained slightly swollen. Her tonsils were very unhealthy.

Grip and power of discrimination were poorer in the left than the right hand. There was a family history of erysipelas affecting her mother, one uncle, one aunt, and a brother. I saw her once again subsequently, when she had had another attack of tonsillitis with *quinsy*, but *no* further phlebitis.

Case 5. *Thrombophlebitis affecting abdominal and pulmonary veins* (April–July 1929).—A burly, broad-chested coal magnate, aged 49, after fishing in Scotland, became shivery and unwell, but decided to travel by road to his home in the south of England. The next day he had epigastric pain.

He arrived home on 28 April 1929 with a temperature of 102° and pain in the upper abdomen aggravated by coughing and deep breathing. *The abdomen* was then soft and *flaccid. By 1 May, however, it* became tense and distended, and there were some rose-coloured spots. At this time attention was focused on his abdominal condition, and a few days later his doctor, Dr. L. Leslie, called in Mr. J. L. Joyce for a surgical opinion. The possibilities discussed included typhoid fever, cholecystitis, pancreatitis, and an inflamed retrocaecal appendix. The pulse-rate did not exceed 76. There was no diarrhoea and no splenic enlargement. Blood cultures remained sterile and Widal's test was negative. Total and differential leucocyte counts showed no abnormality. *By 5 May the temperature was falling.*

On the evening of 6 May he was seized with very severe pain between his left costal margin and the left scapula. At frequent intervals during the next 24 hours he had agonizing constricting pains in the epigastrium, so that breathing was shallow and difficult and he dared not move. Simultaneously the temperature rose to 103° and the pulse to 100. A slight occipital headache transferred itself to the frontal region. Leucocyte count 18,000 cells per c.mm. I saw him at 10.30 p.m. on 7 May with Dr. Leslie and Mr. Joyce. Now and then he *had bad spasms of epigastric pain which caught his breath.* There were no signs of cardiovascular disease. There was general distension of the abdomen, but no spots remained. Excepting for *showing* crowding of the left lower ribs with slight impairment of movement, the physical examination was otherwise wholly negative.

I was asked to see this patient again on 3 June, at the end of the sixth week of his illness. After my previous visit the temperature had at first gradually settled, but then rose again with a return of pain and the development of an effusion at the left base. For a few *days bright blood was expectorated. On 30 May the temperature had* fallen to normal. Two days later it rose again, and on 2 June there was a *slight rigor together with a new agonizing pain below the right* nipple; it is noteworthy that during the previous week the patient had experienced a pain at this point on coughing or sneezing. The condition of the abdomen had improved in the meantime. There was no enlargement of liver or spleen. Blood culture negative. Sputum

examination negative. The fluid previously withdrawn from the left chest was slightly turbid and blood-stained, showing red cells and leucocytes in the deposit, but was sterile on cultivation. A fresh effusion on the right side now gave exactly similar fluid.

I diagnosed wandering pulmonary thromboses. The violent spasmodic pains were exactly like those described in Case 3. The fluid was characteristic of pulmonary infarction and like that obtained in Case 2. The red haemoptysis was typical of infarction. At no time was there anything suggestive of an ordinary pneumonia. I am inclined to the view that the earlier abdominal symptoms were also due to visceral thromboses. Although in the foregoing notes stress has been chiefly laid upon the pulmonary manifestations, it should be mentioned that the advisability of laparotomy was discussed on more than one occasion, and there were several other consultations, at which I was not present, with regard to the proper interpretation of the abdominal symptoms. The patient made a complete recovery.

Discussion

In the group formed by these 5 cases, together with 6 others recently described in some detail in the English literature (Moorhead and Abrahamson 4, Campbell and Morgan 1, Carey Coombs 1), there were 8 examples of pulmonary thrombosis; 4 clear or presumed examples of abdominal thrombosis; 3 probable examples of cardiac and 2 of cerebral thrombosis. Although two of my patients had had anginal symptoms I was not satisfied that these were attributable to coronary thrombosis. In addition to involvement of both upper and lower limbs, Moorhead and Abrahamson also reported cases with thrombophlebitis affecting the face and the abdominal wall.

In those cases in which pulmonary symptoms have followed phlebitis in a limb it might be reasonably suggested that the symptoms were due to small embolisms and not to thromboses. Against this view are (1) the sequence 'left leg, left lung, right foot' in Case 3; (2) the late arrival of the lung symptoms in Case 2; and (3) the occurrence at one period in Case 4 of thrombotic lung symptoms independently of any recent superficial phlebitis. In case 5 there were symptoms of pulmonary thrombophlebitis without any superficial lesion, but there may have been abdominal thromboses. In the case described by Carey Coombs the

because there is no associated septicaemia. The pulmonary thromboses may be heralded by agonizing bouts of spasmodic pain or by ordinary pleuritic symptoms which precede haemoptysis, when it occurs, by hours or days. The association of pleurisy and haemoptysis may lead to an erroneous diagnosis of tubercle. A faintly turbid and blood-stained pleuritic effusion sometimes follows. The abdominal thromboses are characterized by pain and distension and occasionally (vide Moorhead and Abrahamson) by melaena. The symptoms of the cardiac and cerebral thromboses do not differ from similar lesions of other causation, but, as small veins rather than arteries are probably involved, prognosis again need not necessarily be regarded as unfavourable. Treatment is expectant and symptomatic. Liberal fluids and potassium citrate may reasonably be prescribed. Obvious focal infections should receive attention at the proper time. Where the gouty diathesis is present, or may be presumed, a purine-free diet and a liberal fluid intake should be prescribed. Perhaps the most important single conclusion to be drawn from a study of these cases is that thrombophlebitis of this type is to be remembered as an occasional cause of cerebral, cardiac, pulmonary, and abdominal accidents which might otherwise prove difficult to explain.

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XXVIII

NOTES ON PROSTATIC AND GASTRIC URAEMIA[1]

The uraemia which accompanies primary renal disease (chronic interstitial nephritis) is generally accepted as progressive and incurable. There are two varieties of chronic uraemia[2] dependent upon disease remote from the kidneys which, if diagnosed in time, are susceptible of cure. For brevity they may be described as prostatic and gastric uraemia. At present lives are lost through unfamiliarity with the clinical pictures presented by these disorders. Their pathologies are entirely distinct.

Prostatic Uraemia

The majority of patients suffering from the effects of prostatic obstruction find their way to the surgeon. Some of them show, in addition to the bladder symptoms, as is now well known, secondary symptoms due to infection, or to renal embarrassment from 'back-pressure', or to some combination of these. There is, however, a smaller group of cases in which the general symptoms due to renal embarrassment so far outweigh the local symptoms in the minds both of patient and doctor that the advice of a physician rather than a surgeon is sought. Between May 1931 and January 1935 6 cases of prostatic uraemia have been referred to me by six medical men of wide experience, and in each case without the true state of affairs having been recognized. In all of them the subjective symptoms and objective findings were, in fact, sufficient for a diagnosis of uraemia without recourse to laboratory tests. I therefore concluded that the clinical picture of uraemia occurring in the absence of gross abnormalities in the urine was not sufficiently defined or appreciated, and that a brief analysis of these cases might be as useful to others as it has been

[1] *Lancet*, 1935, i. 198.

[2] The acute uraemias accompanying gastric haemorrhage, severe dehydration, &c., are not here under discussion.

instructive to me. One patient was referred for 'anaemia, ? due to a growth'; a second for a bitter complaint of 'dry and sticky mouth'; a third because he looked too ill to warrant some dental extractions advised on account of back pains which were probably a manifestation of his secondary renal disease. In one only had the prostatic obstruction evoked comment, but not so its relation to the general symptoms. In 2 cases an X-ray examination of the alimentary tract had been carried out in the hope of finding an answer to the general and digestive disturbances. In one of these the radiologist had reported (three months before the patient came to me) that the transverse colon was 'elevated by a large cystic swelling'. This was the bladder.

The main clinical features of these 6 cases are recorded in the Table on p. 362. The ages of the patients ranged between 56 and 75 years; the duration of the uraemic symptoms from 'a few weeks' to six months. Symptoms referable to the bladder had been present for a longer period. *None of the patients included his urinary troubles among his leading symptoms.* They were either mentioned as an afterthought or admitted only after direct interrogation. Nevertheless there was a palpable enlargement of the bladder in 5 of the 6 cases, and frequency was present in every case but one. In 1 case there was no albumin in the urine; in the remainder 'a trace' only. The specific gravity, when recorded, ranged between 1065 and 1008. In 1 case there was a gross pyuria, and in 2 'a few pus cells' were noted in the centrifugalized deposit. In the remainder there were either no cells or the specimen was perfectly clear to the naked eye. In no case was peripheral oedema or retinitis observed. The blood-pressure readings varied between 140–90 and 190–125.

Subjective symptoms.—Loss of appetite was constant and sometimes pronounced and was once associated with a disinclination for tobacco. Thirst was pronounced in 4 of the 6 cases. A 'nasty' and a 'salty' taste in the mouth and a 'dry, sticky mouth' were specifically complained of by three patients. Weakness and languor were twice remarked upon and diurnal drowsiness once. Pruritus, nausea, headache,

dyspnoea on effort, cramps, and pains in back and limbs each received a single mention. Some degree of malaise is usual and impairment of mental efficiency and character changes may be noticed by relatives. George Moore in the dedication of his last novel to Sir John Thomson-Walker was eloquent in his description of his own failure of mental power prior to his operation. After the operation he recovered all his old literary ability. Any or all of the symptoms described above would be considered usual in the presence of gross nephritic manifestations, or a markedly albuminous urine. It is in the absence of these that they tend to mislead.

Objective manifestations.—There was loss of weight in every case—in 1 case 'nearly a stone'; in 4 cases half a stone or over; in 1 case 4 pounds. All of the patients looked 'off colour'; 3 showed the slight earthy-brown tint common to other types of uraemic disease. A dry tongue is common. The curious 'fishy' odour in the breath, which has on other occasions helped me to the diagnosis of uraemia, was noted in 3 cases, and in one of these had been remarked by the patient and his wife. Haemoglobin estimations were made in 4 cases, the readings being 48, 60, 65, and 70 per cent. The blood-urea figures ranged from 107 mg. per 100 c.cm. to 288 mg. per 100 c.cm. In the case of No. 2 the reliability of the urea estimation by a technical assistant was called in question. This patient made a full recovery after a two-stage prostatectomy. There was no close correlation between the height of the urea figures and the clinical symptoms or signs, with this exception that the case with the highest figures presented the lowest haemoglobin and was the only one in which vomiting was mentioned. The 'fishy' breath was recorded in the cases with the highest and the two lowest readings. In No. 3 the salivary urea was estimated on account of the unpleasant 'metallic' taste complained of, and gave a figure of 62 mg. per 100 c.cm. as compared with a blood-urea of 97 mg.

Although the blood-pressure was high in 5 out of the 6 cases there was no reason to suspect the simultaneous presence of primary renal disease, the age and earlier history of the patients, the absence of retinitis, and the small traces

of albumin furnishing the chief arguments against this possibility.

In no case was there any account of convulsions. One case is well after a two-stage operation. Two were well some months after the first operation. Two have not been reported. One case died in coma after a first-stage operation. We now believe, from the observations of D. McAlpine[1] and others, that the convulsive phenomena of chronic nephritis are generally expressive not of the intoxication but of the accompanying hyperpiesia and hyperpietic crises of arterial disease. They can occur in cases of hyperpiesia with normal renal function. Conversely cases of prostatic and gastric uraemia, although cramps, muscular twitchings, and coma may supervene, seem little liable to convulsion. Once more it should be emphasized, for it helped to explain why they escaped diagnosis, that for the most part these six patients thought that they were passing plenty of urine. They may indeed pass plentiful, dilute water. As they were troubled with frequency, it had not, with one exception, occurred to them that micturition was seriously obstructed or that they were suffering from actual retention. This lack of appreciation may be due in part to the fact that when a hollow organ becomes gradually and grossly distended it is less able to register discomforts, and in part, perhaps, to the 'dulling' of perception which is a feature of the uraemic state.

The following case is particularly instructive as the patient, although more gravely ill than the others, had noticed no urinary symptoms excepting that he had to pass water once at night.

Case 5. Male, aged 67, complained of recurring attacks of nausea and vomiting during the past 6 months. He experienced no abdominal pain at any time. He had had an X-ray examination of his alimentary tract 3 months previously. He and his wife had noticed a curious, unpleasant odour in the breath. He had been troubled with fidgets and cramps. He had lost half a stone in weight, and there was noticeable wasting about the shoulders. The bladder was distended to the navel. Prostate much enlarged. His blood-pressure was 195–110. Haemoglobin 48 per cent. Urine clear, specific gravity 1008, no albumin or sugar. A few leucocytes but no casts in the centri-

[1] *Quart. Journ. of Med.*, 1933, xxvi. 463.

fugalized deposit. Urine urea 0·85 per cent. Blood-urea 288 mg. per 100 c.cm. After 11 months of suprapubic drainage this patient has recovered his well-being, his weight has risen by 1 st., the haemoglobin is now 80 per cent., and the blood pressure 160–110. The blood-urea, however, is still 116 mg. per 100 c.cm.

The differential diagnosis of prostatic uraemia in the ambulatory phase is from abdominal malignant disease and other causes of anaemia and anorexia appropriate to the sixth and seventh decades.

Gastric Uraemia

This condition is associated with other biochemical disturbances besides nitrogen retention—namely, an alkalosis and a chloride deficiency. It may result from gastric or duodenal ulceration, generally but not always complicated by some degree of stenosis; from pyloric obstruction due to new growth; and from a high intestinal obstruction. Repeated vomiting, vigorous alkaline therapy (particularly in the presence of pyloric stenosis or any associated renal inadequacy), and gastric haemorrhage all tend to encourage alkalosis and uraemia. A raised blood-urea, from twice to five times the normal figure, may also be found in cases of pyloric stenosis when clinical symptoms of uraemia are absent. I have now made it a routine to ask for a blood-urea estimation in all cases of pyloric narrowing, whether benign or malignant, as a high figure calls for special care in respect of pre- and post-operative treatment and anaesthesia.

A valuable group of papers[1] on alkalaemia and renal insufficiency in gastric disease by Hurst, Wynn Houghton, Venables, and Lloyd appeared in the *Guy's Hospital Reports* in 1925, together with references to the English and American literature. Cooke[2] has carefully studied the alkalosis accompanying the alkaline treatment of peptic ulcer. M. Rehfisch[3] has also discussed the gastric and other causes of 'extrarenal azotaemia'.

[1] *Guy's Hosp. Reports*, 1925, lxxv. 147 *et seq.*
[2] Cooke, A. M., *Quart. Journ. of Med.*, 1932, xxvi. 327.
[3] *Lancet*, 1934, i. 78.

Case No.	Age	Bladder symptoms	Duration of uraemic symptoms	Albumin. sp. gr.	Casts	Blood-urea (mg.)	Loss of weight	Anorexia	Thirst	Bad taste	Pigmentation	Fishy odour	B.P.	Haemoglobin (per cent.)
1	75	Nocturia. Palpable bladder.	A few weeks	A trace ?	++	223	Nearly 1 st.	++	−	−	+	−	150/105	60
2	62	"	6 months	A trace 1005	−	?	7 lb.	+	+	+	+	−	175/105	70
3	67	"	2 "	A trace ?	A few pus cells	97	4 "	+	+	+	−	−	180/130	63
4	59	Nocturia.	A few weeks	"	−	143	7 "	+	+	−	−	+	140/90	48
5	67	Nocturia. Palpable bladder.	6 months	− 1008	A few pus cells	283	7 "	Vomiting	−	−	−	+	195/110	
6	62	"	A few weeks	A trace 1008	−	107	8 "	+	+	+	+	+	180/135	

Among 10 cases of gastric uraemia in my own practice there were 6 cases of duodenal ulcer, 1 of gastric ulcer (prepyloric), and 3 cases of pyloric carcinoma. Only one of these had been subjected to intensive alkaline therapy before the onset of uraemic symptoms. Vomiting had been severe before the onset of symptoms in 4 cases, slight in 4, and absent in 1—the case receiving alkaline therapy. Two cases had slight and 1 severe bleeding at the time of development of the uraemic symptoms, or, conversely, bleeding may have occurred in concert with the uraemia. Three cases with duodenal ulceration recovered after operation. One case of pyloric carcinoma survived the relieving gastro-enterostomy with immediate benefit. The remainder died.

The symptoms recorded in this group included mental disturbance, drowsiness, headache, thirst, hiccups, muscular twitching, stupor, and coma. Anorexia, irritability, apathy, and pruritus have also been recorded by others as premonitory of graver trouble. 'Fishy' breath and earthy pigmentation of the face were striking features in one case to be described later. The blood-urea figures in my own series have ranged from twice to seven times normal.

Cases illustrative of various events are described hereunder.

Case 1. *Gastric ulcer with fatal alkalosis and uraemia.*—Female, aged 30. This patient, whose case was previously reported by Wynn Houghton, was admitted to hospital for vomiting, without pain. She was found to have 8 hours' gastric stasis by the barium meal but without a visible lesion; she was promptly relieved by gastric lavage. She was readmitted later with a return of symptoms, became mentally peculiar and emotional, and finally stuporose, and died. The blood-urea was two and a half times normal. There was no albuminuria at first, but albumin and casts appeared shortly before death. At the autopsy a prepyloric ulcer, which was not encroaching upon the sphincter, and a mild gastritis were the only pathological findings. The kidneys were normal to naked-eye inspection.

Case 2. *Duodenal ulcer with stenosis; alkalosis and uraemia immediately following gastro-jejunostomy; recovery.*—Male, aged 51. Gave a 20 years' history of dyspepsia. Eight years previously he had been *operated on for a perforated duodenal ulcer. Two years before he was* referred to me by Dr. Bernard Haigh he started alkaline treatment, taking a quarter of a pound of Maclean's powder each week. Recently

he had complained of copious acid vomits and had lost nearly 2 st. in weight. There was visible peristalsis. In addition he showed slight hyperthyroid symptoms and a blood-pressure of 200–120. He was admitted to Guy's Hospital, where the diagnosis of pyloric stenosis from a chronic duodenal ulcer was confirmed. Mr. Philip Turner operated, performing a short circuit. Shortly after coming round from the anaesthetic he became restless and mentally peculiar, and finally stuporose. However, with salines and sedatives he recovered. The blood-urea was 112 mg. per 100 c.cm. He had not been having intensive alkaline therapy before the operation, nor had he complained of general symptoms, or been noticed to be peculiar in any way. With a blood-urea estimation prior to operation it is possible that this anxious episode might have been avoided.

Case 3. *Duodenal ulcer without gastric stasis; alkalosis and uraemia following alkaline therapy; recovery; gastro-jejunostomy.*—Male, aged 43. Had suffered in earlier life from bilharzia and pulmonary tuberculosis. Intermittently over a period of 6 years he had been troubled with symptoms of duodenal ulcer, usually responding promptly to diet and strict treatment. In June 1933 he had a vomiting attack with a slight haematemesis. He then remained fairly well until the beginning of December 1933, when he had another small haematemesis. He was put to bed and given frequent doses of Maclean's powder. I saw him on 11 December when he was looking very ill, drowsy, apathetic, with a brown-tinted complexion, dry tongue, and 'fishy' breath. He was admitted to a nursing-home where he remained very drowsy for some days. He complained of slight headache and had to be roused to talk or to take his feeds. There was pronounced thirst. Urine plentiful, with only a haze of albumin, probably due to a chronic cystitis with pyuria. Previously his renal function was known to be satisfactory. Blood-pressure 140–90. Alkalis were immediately stopped. The blood-urea figure was 175 mg. per 100 c.cm. He slowly improved. After 6 weeks the blood-urea had fallen to 58 mg. per c.c., but gastric symptoms had again become troublesome and feeding was difficult. No gastric stasis was demonstrable radiologically. After preparation with continuous intravenous saline a *gastro-jejunostomy was performed by Mr. L. Bromley in* February 1934. Convalescence was slow but immediate recovery complete. Later recurrences of gastric symptoms with perforation led to further surgery and ultimately to a partial gastrectomy.

Case 4. A man, aged 68 years, had been troubled for upwards of 20 years with gastric symptoms of which vomiting, coming in attacks but with free intervals, had been the outstanding symptom. Gastric stasis up to 9 hours, as shown with the barium meal, had been reported a year previously and a test-meal had shown hypersecretion. Operation had been declined. I saw him with Dr. Allen on 4 February 1935.

A week previously he had had a vomiting attack and was given alkalis but not in large doses. On 31 January the vomiting had stopped but he felt ill in himself. In the 48 hours preceding the consultation he had become drowsy and thirsty with a dry tongue and slight twitching of the limbs. He was just able to answer questions, but was very confused. There was an visible dilatation of the stomach, no peristalsis or splash, but I noted marked resistance in the right upper quadrant. The urine showed a very slight haze of albumin; no casts. The blood-urea was 140 mg., but the urine contained 3 per cent. of urea. A diagnosis of pyloric stenosis from an old duodenal ulcer with 'gastric uraemia' was made. It was decided, in consultation with Lord Horder and Mr. W. H. Ogilvie, that in his present state operation was out of the question. His stomach was washed out and he was given continuous intravenous glucose-saline, taking approximately 10 pints in 48 hours. His subsequent blood-urea figures were as follows:

6.2.35	75 mg.
9.2.35	65 mg.
13.2.35	60 mg.
18.2.35	55 mg.
20.2.35	50 mg.

After the first few days fluid mouth-feeding, without alkalis, was reinstituted. On 18 February vomiting started again. On 19 February gastric lavage brought away 450 c.c. of dark bilious fluid. On 20 February, under morphine and splanchnic block anaesthesia, Mr. Ogilvie operated. He found a large inflammatory mass beneath the liver and involving the duodenum and performed a gastro-enterostomy. The patient made a good recovery and left the nursing-home on a light mixed dietary on 29 March 1935. His last blood-urea figure, on 5 March, was 49 mg.

Whatever part the associated alkalosis and chloride deficiency may play in these cases it will be seen that the clinical picture of gastric uraemia includes symptoms common to nephritic and prostatic uraemia. These common symptoms may indeed be regarded as the true symptoms of uraemia. I have not encountered any case of gastric uraemia with convulsion. Tetany, which was formerly regarded as an important nervous manifestation of pyloric obstruction, has not, so far as I can recollect, been recorded among any of my private or hospital cases of ulcer or cancer in recent years. Seen in the stage of coma with a normal urine and an indefinite gastric history the diagnosis of gastric uraemia may present great difficulties.

Treatment

The treatment of *prostatic uraemia* is mainly a matter for the surgeon. It includes careful 'decompression' of the distended bladder, a two-stage operation, and treatment of the anaemia.

The treatment of *gastric uraemia* includes the prompt withdrawal of all alkalis, gastric lavage, rectal salines, and, in grave cases, or as preparation for operation in cases with a high blood-urea, intravenous salines by the continuous method, and finally appropriate surgery. With extension of the knowledge that uraemia may be due to extrarenal causes, prostatic and gastric uraemia should commonly be preventable.

XXIX

MYXOEDEMA AND OTHER MANIFESTATIONS OF THYROID DEFICIENCY[1]

In the case of the patient whom I bring before you I will reverse the usual order of procedure, and before considering her history and symptoms, ask your attention to certain physical features, and particularly to her facial appearance. Physiognomical diagnosis is an important chapter in clinical medicine, and becomes steadily more so as we turn the pages of experience. There are few cases in which the face will tell us nothing. There are some in which it tells us almost everything we need to know. In acromegaly, myxoedema, Graves's disease, in some cases of tabes dorsalis, in the Parkinson's mask of paralysis agitans and encephalitis lethargica, in pernicious anaemia, in the Hippocratic facies of grave abdominal disease, and in the mitral facies we have well-known examples of 'diagnostic physiognomies', and the list might be considerably extended. Not infrequently the countenance of disease will guide us to a correct opinion when the physical overhaul or the tale of symptoms *is* unconvincing. In examining facial characters we take into account the general conformation and proportions, the colouring and nutrition, the texture of the skin, the expression, and the distribution of the hair, any or all of which may show some significant change.

You will doubtless be chiefly impressed by the anaemic appearance of this patient, but note how broad her features are, how placid and immobile and lacking in any play of emotion. Although there is a marked underlying pallor, with a slightly yellow tint, the cheeks are peculiarly pink. The skin is smooth, like china. The eyebrows are scanty, and the hair-margin has so far receded towards the vertex that she has found it necessary to arrange her coiffure so as to hide this deficiency. When I try to pluck up the skin of

[1] *Guy's Hosp. Gazette*, 1930, xliv. 123.

the forehead I find this almost impossible on account of the thickness of the skin, and on taking the tissues of her cheeks between a finger and thumb a feeling as of some firm infiltration is imparted. These are the facial characters of myxoedema, and although in her case there are some additional findings, including a large spleen, which have suggested the possibility of a mixed pathology, they justify, when taken in conjunction with her own complaints, a fairly confident diagnosis.

Our patient is aged 42 and married. She has had 5 children and 2 miscarriages. Fifteen months ago she noticed that she was getting pale, and since then there has been increasing loss of energy and dyspnoea on exertion. Her hair has been getting thinner. She does not sweat as readily as she used to do. She prefers the warm weather. Her weight has not altered appreciably. In the ward we have been struck by her slow speech and her impassive behaviour. Her voice is husky at times. She has a broad and rather smooth tongue, and on account of this smoothness and her anaemia and the enlargement of the spleen the possibility of pernicious anaemia had been discussed. However, the blood count shows a microcytic anaemia, with haemoglobin down to 25 per cent. and a colour-index of 0·3. She does not show the slowing of the pulse and markedly subnormal temperature frequently manifest in myxoedema.

Before passing to a more general discussion of the disease and its differential diagnosis and treatment, I should like you to listen to the histories of two other patients. In these cases the diagnosis was further confirmed by the response to treatment—a confirmation which we have still to obtain in the case before us.

Case 1. Mrs. N—, aged 42, was admitted on 23 February 1923. Her mother died of consumption. She had two daughters living, aged 21 and 19 years. Two other children died in infancy. Twenty-two years ago she had enteric fever. Before this date she enjoyed perfectly good health, but she has never felt really fit since the illness. In 1911 she had pneumonia, and six months later was operated on for appendicular abscess. These two illnesses further aggravated her feelings of unfitness. For 12 years she has noticed gradually increasing muscular weakness, with impairment of memory and slowness of

speech. She has also experienced an increasing intolerance for cold, and feels chilly even in summer. In recent years she has been growing fat, though latterly she has again lost weight. She has noticed puffiness of the face and eyelids and dryness of the skin. She never sweats. Recently she has had to give up her household duties on account of weakness. She frequently forgets what she wants to say, and whereas she used to be 'sharp-spoken', she is now 'very slow'. Her hair has been falling. The periods have been irregular. She was sent to Guy's, however, not so much for these general symptoms as for some vague abdominal discomforts, for which she was seen by Mr. Turner. He considered that these symptoms could be sufficiently accounted for by visceroptosis, and was struck by her general condition. He drew attention to the hyperaemic patches on her cheeks, which suggested mitral stenosis. These were a striking feature, contrasting sharply with her rather yellowish underlying pallor. Even more striking, however, was the general heaviness of the features, and the complete absence of any play of emotion or expression in the course of the interrogation. The eyelids were slightly puffy. The hair was dry and coarse, and the outer half of the eyebrows was lacking; the hair-margin had considerably receded. Her voice was monotonous, and her words were uttered slowly. Her latent period in answering questions was longer than normal. The integument of the forehead was thick. The skin was everywhere dry, and the axillary hair was scanty. Her pulse was 64, temperature 97·4°, and respiration-rate 20. The systolic blood-pressure was 135. The blood showed a haemoglobin percentage of 65, and a red cell count of 4,140,000. The basal metabolic rate was minus 24·7 per cent. Glucose tolerance was, however, normal. It should be mentioned that she had been taking small doses of thyroid while awaiting admission. She was treated with thyroid in the form of Tab. Thyroid (B. & W.), and seemed to do best on a dose of gr. 2 thrice daily. This represents only about gr. 1½ of dried thyroid in the day. She improved steadily, and a few months later, excepting for a slight tendency to dizziness, had lost all her symptoms. Her colour had improved remarkably. In figure she became slim and sprightly. Her face and expression were happy and vivacious.

Case 2. Mr. M—, aged about 50, was admitted on 30 April 1923. He complained of 'debility and noises in the head'. In 1911 he became gradually weak in his legs and arms, and after the slightest exertion he felt exhausted and tired. In 1919 he felt much worse and was admitted to St. Bartholomew's Hospital. He says that he was treated there for 'septic anaemia and liver trouble' for which his teeth were extracted. He has, however, remained incapable of any sustained effort; has felt the cold severely; his bowels have been constipated, and he has continually felt weak and tired. Latterly his memory has been defective.

He looked very different from the patient just described, and yet

his appearance at once suggested myxoedema. He was not fat, and did not show the patch of malar hyperaemia; nevertheless his face was expressionless; his forehead was corrugated and stiff, but smooth and shiny between the wrinkles; his hair was sparse, and felt curiously dry and coarse when rolled between the fingers, and was altogether lacking in gloss. His face had a yellowish tinge; on the trunk the skin was scaly and dry; sweating was entirely absent; the wrinkled skin of his neck was reminiscent of the tortoise; his speech and movements were laborious and slow. The first time we examined him at the bedside the sister said, 'Would you like to see him take his own shirt off?' She had recognized that this leisurely act was a demonstration in itself. His haemoglobin was 78 per cent.; his red cells 3,740,000. His basal metabolic rate was nearly 50 per cent. below normal. Before treatment his daily metabolism amounted to only 805 calories. A month later, after treatment with Tab. Thyroid (B. & W.) rising to *gr. 8 per day, his daily metabolism amounted to 1,480 calories—still* a low figure.

Aetiology and General Features

Myxoedema is a disease of adults, and occurs for the most part in women shortly before, during, or after the menopause. Seven women are affected for every one man. One-half of the cases occur between the ages of 30 and 50. No definite predisposing factors are known, but sometimes, as in Case 2, the symptoms seem to have developed insidiously after a severe illness.

The symptoms are those which one would expect from a general depression of metabolism, but we may go further and say that there is no vital function which may not share in the depression. Weight is frequently, but not always, increased; fatty pads may develop above the clavicles; the pulse is slow; the temperature is subnormal; the patients nearly always complain that they feel the cold much; the skin is dry, the hair coarse and scanty; the eyebrows are commonly deficient in their outer half; the nails are brittle, and the bowels costive. Movements and speech are slow and lack expression. The voice may be husky, and in advanced cases dwindles to a croak, owing to submucous infiltration of the vocal cords. The facies often betray the diagnosis directly the patient enters the room. No emotion

seems to light up the features during conversation, and a smile, if it appears, is slow to develop. The face, contradictory though it may seem, is both abnormally smooth and wrinkled. The smoothness, as depicted by Gull, resembles porcelain, but around the eyes and mouth are frequently to be seen numerous fine wrinkles. The eyelids are thick and puffy and look oedematous, or as though they had recently been oedematous. Nephritis may suggest itself at the first glance, or a suspicion of mitral disease may be entertained on account of the peculiar patch of purplish-pink hyperaemia the upon cheeks—'the cheeks tinted of a delicate rose-purple' (Gull). The hands are coarse, and sometimes referred to as spade-like. The legs may appear infiltrated, but unless the disease is complicated by renal inefficiency or severe anaemia, there is no pitting on pressure. The urine contains no albumin. There may be a slight or sometimes a severe anaemia of the secondary type—a feature not always sufficiently stressed, which led to the suggestion that the thyroid gland might be a haemopoietic organ. More rarely there is a macrocytic anaemia. The psychology of these cases no less than their physique is affected. In the earlier stages the patient notices her langour and disinclination for mental effort and concentration. Later this becomes obvious to all, and she is heavy and unresponsive and her speech is slow and toneless. The memory becomes poor. Nothing is more remarkable in the general improvement under treatment than the return of vivacity, the altered timbre in the voice, and the recovery of mental alertness and elasticity. Amenorrhoea is often present in cases developing prior to the menopause, although sometimes there is irregular or excessive loss. Menstruation may reappear under treatment, and it is stated that, after a *period of sterility, fertility has been re-established.* By estimations of the basal metabolic rate determination of the degree of hypothyroidism has become possible. But an adequate estimate of this and of improvement under treatment may be obtained by observations of the general symptoms, pulse and respiration rates, temperature curve and weight.

Differential Diagnosis

In a fully developed case the diagnosis of myxoedema should not be difficult, and yet there are four conditions for which it is not infrequently mistaken.

The first is *mitral stenosis* or *other heart disease*—on account of the purplish malar hyperaemia. A woman, aged 69, came to see me, looking so ill and sallow and with such a purple hue to her cheeks that I could well understand why she had been kept in bed for some weeks as a case of heart disease. Her complaint of great weakness and some dyspnoea lent additional weight to the opinion. However, I could find no sign of cardiovascular disease, and she showed many other stigmata of myxoedema. She was restored to active health by thyroid treatment.

It should, however, be mentioned that a genuine condition of 'myxoedema heart', with myocardial changes clinically and cardiographically manifest, has been described. Dr. J. M. H. Campbell gave a good account of this condition in the *Guy's Hospital Reports* for 1934.

The second is *pernicious anaemia*. Confusion occurs, first because myxoedematous patients may show a 'yellowy' anaemia, not unlike the lemon tint of the other disease; secondly, because patients with pernicious anaemia not uncommonly present a smooth skin and other facial features a little suggestive of thyroid deficiency. Perhaps the activity of the thyroid gland is actually subnormal in virtue of the anaemia. Finally there may be a macrocytic anaemia in association with myxoedema and requiring liver therapy in addition to thyroid medication.

The third is *nephritis*, because of the pallor and puffiness, but the absence, as a rule, of true oedema and albuminuria makes the distinction.

The fourth is *neurasthenia*—an old enemy to precision in diagnosis. One of the worst cases of myxoedema in a male which has come my way was that of a man in middle life who, for upwards of 10 years, had slowly been losing mental and physical energy until he was almost incapacitated. He had been given the label of neurasthenia. His harsh, dry

skin, his weary voice and slow speech, his thick winter underclothing worn in midsummer suggested the diagnosis. His case demonstrates a real difficulty in diagnosing myxoedema, namely, its slow course and insidious advance. Three of the cases I have described gave histories of ten years or more. It is thus easier, sometimes, for the consultant or some one who has never seen the patient previously to form his opinion than for the family doctor, who must endeavour to assess the meaning of subjective symptoms, often indefinitely stated by the patient, and remains unimpressed by physical or physiognomical changes by reason of the very slowness of their arrival during a period, not of weeks or months, but years.

Treatment

Apart from general hygienic measures, treatment may be condensed into the one word, 'thyroid'. The dosage varies with the case, but large doses are rarely necessary. The response to treatment becomes apparent within about three weeks. It is well to remember that most of the proprietary preparations have their dosage expressed in terms of fresh gland, and that gr. 5 of Tab. Thyroid (B. & W.), for instance, is therefore equivalent to gr. 1 of Thyroid. Siccum (B.P.). I seldom find that more than gr. 3 daily (or its equivalent) of Thyroid. Siccum are necessary to control a fully developed case. Occasional adjustments of the dosage may be necessary, but the administration must be continued for the rest of the patient's life. Iron or liver may also be necessary.

Some Other Manifestations of Thyroid Deficiency

1. *Minor hypothyroidism.* For every case of developed myxoedema which you may see, and as such it is a rare disease, you will see many cases of minor hypothyroidism. In women of a particular type it is not uncommon for dryness of the skin, brittleness of the nails, falling of the hair, and a gain in weight to accompany or follow the menopause, and small doses of thyroid may here have a beneficial effect. Obesity, without other signs of hypothyroidism, is not generally an indication for thyroid treatment.

2. *Creaky knees.* Some years ago Mr. E. G. Slesinger drew my attention to a type of arthritis affecting the knees only, and occurring in women at or after the menopause. I have been accustomed to label the condition 'creaky knees'. At times it causes considerable disability, with stiffness, weakness, pain, and not a little thickening of the joints The patients are particularly aware of their disability in going downstairs or getting up out of a low chair. They generally show some slight evidences of hypothyroidism, and are often, but not always, overweight. Mr. Slesinger told me that they frequently improved in a striking way under thyroid treatment and I have many times confirmed the observation. The improvement in local symptoms and signs is remarkable, and this simple measure may succeed when others have been tried and failed. I do not think the effect can be wholly accounted for by lessened articular stress through loss of weight.

3. *Sterility.* I was once consulted by a married woman in the thirties for general unfitness and dyspepsia. She also confessed that for years she had been hoping in vain for a baby. She had an exceedingly dry skin. Her health improved under thyroid and she later reported that her wish had at last been fulfilled. On one other occasion I have recorded pregnancy following thyroid treatment for hypothyroidism. I think it not improbable that the thyroid was responsible, but you must not expect thyroid to bring about this happy result unless there are other indications of defective thyroid secretion.

4. *Chronic oedema.* A spinster, aged 66, consulted me for extremely thickened, stiff, and creaky knees. In addition both her legs were enormously swollen with a true but very solid oedema, so that their appearance suggested elephantiasis. To this condition she had become resigned as she had had it for many years; in fact, she had consulted Guy's physicians of two previous generations about it. Mentally she was very active and alert, and although very stout, she did not show other signs of hypothyroidism. I prescribed thyroid because of the creaky knees, and to her great pleasure and my surprise, remarkable improvement followed

not only in respect of the knees, but also in respect of the oedema, which gradually melted away. She lost 3 st. in weight and the circumference of her ankles was reduced from 13½ to 9½ in. This was one of those happy and unexpected results we meet with from time to time, but it followed upon a treatment not without a rational basis.

In conclusion I would remind you of some historical points concerning myxoedema. It was first described by a Guy's physician, Sir William Gull, who in 1873 read a paper before the Clinical Society of London 'On a Cretinoid State supervening in Adult Life in Women'. He depicted all the essential characters of the disease, and no one has improved upon his clinical portraiture. The morbid anatomy and histology were described four years later by William Ord, who refers to the 'jelly-like swelling of the connective tissue, chiefly, if not entirely, consisting in an overgrowth of the mucus-yielding cement'; he also proposed the name of myxoedema. Hilton Fagge, in a paper on 'Sporadic Cretinism' (1871), had already associated the physical changes with atrophy of the thyroid gland. In 1892 Hector Mackenzie showed that thyroid feeding would cure the disease.

XXX

MENINGITIS AND MENINGISM[1]

Some of you will remember having seen in my wards during the early weeks of the present year two cases of meningitis in small children, the one meningococcic and the other tuberculous, the first progressing satisfactorily to recovery after treatment with serum; the second, as was inevitable, ending fatally. Shortly afterwards I saw elsewhere, in quick succession, two further cases presenting the syndrome of meningeal irritation, but in neither case as a result of meningeal infection. This small group of cases not unnaturally set me thinking of the various conditions in which I had encountered the signs and symptoms commonly considered as peculiar to meningitis. It occurred to me that it might not be amiss to do some of this thinking aloud at a clinical lecture.

I propose to give you, first of all, a brief account of these four cases, together with a description of four others from among my files; secondly, to consider how far the case-histories were in agreement, in what respects they differed, and what were the points of differentiation which led to the final diagnosis in each instance; and, thirdly, to extract from the whole series a common group of symptoms with a view to deciding, so far as we may, their specific import.

By way of introduction, let me remind you that we generally mean by the term 'meningitis' a pathological state involving inflammation (generally an infective inflammation) of the meninges, and by 'meningism' a clinical state suggestive of meningitis, but lacking such final proofs of meningitis as an increase in the cellular content of the cerebrospinal fluid or the presence of organisms. As I shall hope to show, these terms, although sometimes used by the physician in a differential sense, are not contradistinctive, for every case of active *meningitis manifests meningism* and (although this might not be so universally approved)

[1] *Guy's Hosp. Gazette*, 1932, xlvi. 123.

every patient with meningism has, I believe, irritation of his meninges or a mild meningitis, even though this be not due to the presence of bacteria or proclaimed by the visible products of bacterial inflammation.

What are the symptoms and signs which accompany meningism and meningitis? Severe headache generally, photophobia frequently, vomiting not infrequently are among the patient's complaints. The vomiting and headache are probably symptomatic of the increased intracranial pressure rather than of the local inflammation of the membranes. Neck-rigidity in some degree, with head-retraction in extreme cases, and a positive Kernig's sign are the most important physical signs. Neck-rigidity is best tested for by inserting the fingers of the two hands behind the occiput of the patient and gently attempting to raise the head from the pillow so as to approximate the chin to the chest. Any pain so caused will be immediately apparent in the patient's face. Objectively there is a sensation of stubborn stiffness or involuntary resistance, and the intended approximation of chin to chest is found to be prevented in varying degree. To elicit Kernig's sign we flex the thigh to a right angle with the trunk and then gently straighten the leg on the thigh. In a healthy child the leg will easily straighten completely. In older subjects it will, at any rate, extend sufficiently to form a wide obtuse angle with the thigh. When the sign is positive a sense of fixed resistance, sometimes almost suggesting ankylosis, is felt as the knee reaches or just surpasses a right angle. If the pressure is continued pain is caused and the other leg is sometimes involuntarily flexed. Both with neck-rigidity and Kernig's sign there is some correspondence between the activity of the inflammation and the positiveness of the sign.

Now let us turn to our cases.

Case 1. A male baby, aged 9 months, was admitted to Mary Ward on 28 December 1931 with high fever, up to 106°, and rapid respirations. We were anticipating pneumonia, but no localizing signs appeared until the fifth day, when convulsive twitchings of the right side and transient strabismus were noticed and a slight degree of neck-rigidity and Kernig's sign were demonstrated. A faintly turbid cerebrospinal fluid under increased pressure was withdrawn

by Mr. G. V. Steward, and the laboratory reported a polymorphonuclear increase and meningococci. Anti-meningococcal serum was given on six occasions intrathecally and the child made a good recovery, complicated only by acute iritis with haemorrhage into the anterior chamber of the left eye. The history and course of this case suggest a meningococcic septicaemia with a delayed meningeal localization producing only moderate symptoms. In the majority of cases of acute meningitis (whether meningococcic, pneumococcic, or streptococcic) the physical signs are more pronounced than they were in this case.

Case 2. A boy, aged 9, was admitted to Addison Ward on 14 January 1932 for fever and profound lethargy. His earlier life had been healthy excepting for winter cough. At the end of November 1931 he sustained a slight concussion. He was then well until Christmas, when he had pleuritic pain in the left chest. On Christmas Day he was quite happy, but on 27 December he was quiet and feverish, and thereafter remained subdued until 11 January, when he began to complain of occipital headache. On 13 January a lumbar puncture was performed by Dr. W. F. Hudson, of Banbury. On admission, he lay flat on his back with his eyes half-closed. Neck-rigidity and Kernig's sign were present, but in very slight degree. The abdomen was retracted. He resented examination, and when his night-shirt was raised to allow examination of the abdomen he tried to pull it down again with an irritable protest and grimace, exhibiting what has been described as 'Stocker's sign'. James Stocker, who was apothecary to Guy's Hospital for many years until shortly before his death in 1878, pointed out that this type of irritability distinguished cerebral cases from cases of illness with apathy due to the then prevalent 'fever'. The cerebrospinal fluid was under pressure and clear, and an excess of lymphocytes with tubercle bacilli was reported. The boy became comatose with high pyrexia, and died on 21 January 1932.

The mode of onset was very different in these two cases, acute with high fever in the first, insidious with increasing stupor in the second. The neck-rigidity and Kernig's sign were not pronounced in either, but less so with the less fulminating infection. The decubitus and Stocker's sign were most characteristic in the boy with tuberculosis, and the earlier history of a pleurisy gave evidence of the primary lung focus, later revealed at the post-mortem examination.

Case 3. In January 1932 I saw, with Dr. G. E. W. Lacey, a nervous and childless married woman, aged 42, who gave the following story. She had always been liable to headaches and fainting. In the previous week she had been busy looking after neighbours with influenza. Three days before the consultation, while at stool, she was suddenly

seized with intense pain in the head. She managed to get to her bed and there lay, apparently unconscious, for 2½ hours, and 2 hours later she was still stuporose. The knee-jerks were exaggerated, and Dr. Lacey queried a left extensor plantar response. The temperature on the first day was 99. When I saw her she was rational and afebrile, but still complaining of headache. There was a slight but definite neck-rigidity with a positive Kernig's sign. The left plantar response was definitely extensor. Her blood-pressure was 200–130. She recollected that 3 months previously, when scrubbing a floor, she had been seized with a similar headache, which lasted some hours. I diagnosed 'sub-arachnoid haemorrhage', and, as she was so clearly improving, decided against a lumbar puncture. The absence of pyrexia after the first day and of serious constitutional disturbance opposed any acute form of meningitis, and the high blood-pressure suggested the more probable pathology.

Case 4. A prosperous business man of plethoric type, who was known to have a high blood-pressure, was noticed one evening to be a little peculiar in his behaviour. The next morning he vomited three times in quick succession and was dazed. He was put to bed and remained there in a semi-stuporose condition for the next ten days. When I saw him, in consultation with Dr. W. J. Montague, he was lying with his hand pressed to his forehead, but did not admit to much pain. He was restive at night and required catheterization. His temperature fluctuated between 99 and 101. There was distinct neck-rigidity with a positive Kernig's sign. We also noticed a slight weakness of the right arm and leg as compared with the left, and the finger-nose test was performed badly with the right hand. A lumbar puncture performed by Dr. Montague before my arrival showed an intimately blood-stained fluid, the blood being largely laked. The blood-pressure was 190–110. Here the diagnosis of hyperpiesia with sub-arachnoid haemorrhage was confirmed by the lumbar puncture.

Sub-arachnoid haemorrhage occurring spontaneously in a patient with high blood-pressure is less likely to give rise to difficulties than the same accident in a child or young adult. Here, as Sir Charles Symonds[1] and others have shown, the haemorrhage usually comes from a small aneurysm, either congenital or, in cases with infective endocarditis, resulting from embolism.

Case 5. In 1929 I saw at the Blackheath and Charlton Hospital, with Dr. R. W. Warrick, a boy, aged 14, who had been found unconscious in the lavatory 4 days previously. On admission, neck-rigidity was discovered and a lumbar puncture had been performed, giving a

[1] *Guy's Hospital Reports*, 1923, lxxiii. 139.

blood-stained fluid with no organisms. On recovering consciousness, he was found to have a right hemiplegia. Slight pyrexia continued for the next 3 days. Neck-stiffness and Kernig's sign were well marked at the time of my visit. I noticed weakness with increased reflexes of the right arm and leg and a right extensor plantar response. The cerebrospinal fluid that day was pale yellow and showed an increase of protein. The boy's previous good health, the abrupt onset and localizing signs, and the changes in the cerebrospinal fluid made a leaking congenital aneurysm an almost certain diagnosis. Within a few days of the accident he was cheerful and able to take food in a way which would have been most unusual in a child with meningitis.

Here, then, we have three cases of haemorrhage on the surface of the brain causing the same leading symptoms which we have just considered in cases of infective meningitis. With a widely differing pathology we find headache, fever, neck-rigidity, and Kernig's sign common to these conditions. I may remind you that haemorrhage into other serous cavities, such as the peritoneum or a joint, may also closely simulate inflammation of their membranes. You will observe that in each of the cases of meningeal haemorrhage some additional feature, such as abrupt onset (in two cases in the lavatory), high blood-pressure, or some indication of local cerebral damage was present to help in the differentiation from infective meningitis.

Case 6. In May 1928 I saw on the tenth day of his illness, with Dr. J. W. Ensor, a boy of 17 years who had complained primarily of headache, which later became severe and was associated with pain and stiffness in the limbs. On the fifth day he tried to get out of bed and found that his legs would not support him. His temperature, which never rose above 101, was normal on the seventh day. The headache had departed, but I still found well-marked neck-stiffness and Kernig's sign. In addition, however, he had a flaccid weakness of both quadriceps with absent knee-jerks and left ankle-jerk and absent abdominal reflexes. The case was one of anterior poliomyelitis.

The cerebrospinal fluid in acute poliomyelitis frequently shows a lymphocytic increase. We have here another example (although the main incidence of the disease is on other parts) of infection of quite another type which sometimes affects the meninges.

Case 7. A young nurse was admitted to Mary Ward with general superficial adenitis due to an accidental infection with syphilis. After her first dose of N.A.B. she developed acute cerebral and meningeal

symptoms, including severe headache, neck-stiffness, convulsions, and a slow pulse. The cerebrospinal fluid showed an excess of lymphocytes. Later she developed a right-sided hemiplegia. After a long illness and intensive treatment with mercury, iodides, and bismuth, all signs eventually cleared up. The Wassermann reaction of blood and fluid became negative, the cell-count became normal, and she was able to return to her work and has since kept well.

This is not a common story. I mention it merely as an example of one other type of infection which may give rise to meningitic manifestations when abruptly activated.

Case 8. Lastly we come to a case of what would be styled 'meningism' in the more accepted sense of the term. A year ago a small boy was admitted to one of my cots in Mary Ward. In the surgery his symptoms were mainly abdominal, and appendicitis had been suspected. Shortly after admission he developed neck-rigidity and Kernig's sign. He may be said to have shown 'peritonism' and 'meningism' in quick succession. He then developed signs of an apical pneumonia and, later, an empyema, and finally acquired scarlet fever and died in the isolation room. A lumbar puncture performed during the stage of meningism showed that the fluid was under definitely increased pressure but there were no cellular abnormalities.

Meningism of this type is a not infrequent occurrence in children with pneumonia or otitis media. That the nervous system in childhood is a more sensitive machine is shown by the frequency of convulsions in the tender years. Although I was frequently compelled to perform a lumbar puncture in cases of typhoid fever and trench fever during the 1914–18 War on account of intense headache and a pseudo-Kernig's sign due to muscular pain and stiffness, I cannot recollect that I have ever seen pronounced meningism apart from meningitis or meningeal haemorrhage in an adult.[1]

Now if we are to accept, as seems reasonable, that the meningism (i.e. Kernig's sign and neck-rigidity) in cases 1 to 7 was expressive of a genuine meningeal inflammation, it becomes difficult to believe that the indistinguishable meningism of pneumonia and otitis media in children can

[1] Since this lecture was given we have had a case in Clinical Ward of a man with an epidural abscess who showed meningism. His cerebrospinal fluid was under increased pressure, but quite clear. It showed no organisms, but an increase both of polymorphonuclear cells and of lymphocytes. He had, therefore, a mild meningitis due to a neighbouring infection. Later he succumbed to a septic meningitis.

have an alternative explanation. And yet it is, I fancy, quite commonly supposed that meningism of this type is due to some vague 'reflex irritability', or else the syndrome is left unexplained. Is it not too readily assumed that an absence of cells and organisms or a negative inspection after death establishes the absence of meningitis? I would rather argue that meningism is a specific reaction more delicate in its proclamations than the pathologist's microscope, and that there is a genuine irritation, or non-infective inflammation, of the meninges in these pneumonic and otitic cases due, probably, to the chemical products of fever or contiguous infection. We have further observations in support of this. In one case described (Case 8), although there was no cellular increase the pressure of the cerebrospinal fluid was conspicuously raised. If the pressure of the fluid is raised, there must either be some process stimulating an increased secretion or some interference with absorption. In other serous cavities of the body, such as the knee-joint, we know that effusion may occur without the presence of bacteria or leucocytes. Furthermore, I can relate another case of meningism with pneumonia in a child in which, with a clear fluid, we yet discovered a few polymorphonuclear cells in the centrifugalized deposit, and an adult case of presumed meningitis in a soldier in which one colony of meningococci grew from a clear fluid and the patient proceeded to get well after a single puncture. Findings such as these seem to me to establish the link between the cases of supposedly non-meningitic meningism and the cases with accepted proofs of meningitis. With the help of such observations may we not argue that meningism (that is to say, the syndrome including neck-rigidity and Kernig's sign) is always specific of meningitis, even if that meningitis, as in the case of sub-arachnoid haemorrhage and the pneumonic and otitic forms, is an aseptic meningitis and unassociated with gross products of inflammation in the cerebrospinal fluid?

While they are specific of meningeal irritation, the symptoms of meningism are not, however, specific of any type or cause of irritation. *This is true of all well-defined symptoms.* They constantly specify a type or mode of physiological

disturbance, but they do not in themselves indicate the particular cause of the disturbance. For a full diagnosis other clues must be sought in the age and the general condition of the patient, in the history, and in associated symptoms and signs.

In conclusion, there are four main groups of cases in which meningism may be observed:

1. Acute pyogenic meningitis (meningococcic, pneumococcic, streptococcic).
2. Sub-acute meningitis complicating general tuberculosis, poliomyelitis, or activated syphilis.
3. The aseptic meningitis of sub-arachnoid haemorrhage.
4. The meningeal irritation or aseptic meningitis of pneumonia and otitis media in children.

With ordinary clinical care it should be possible to place a case in one of these four groups, and often enough to give a correct opinion. With the aid of the lumbar puncture needle an accurate diagnosis can generally be established.

XXXI

SOME ALARMING SEIZURES[1]

In the course of medical practice we are confronted from time to time by peculiar 'seizures' or 'nerve storms', which lack conformity with the more familiar descriptions. Some of these seizures cause great alarm to their victims, in that they seem to threaten paralysis, speechlessness, unconsciousness, or even death itself, or because they occasion states of profound instability and prostration. The appearance and sufferings of the patients during these attacks may further alarm relatives or onlookers, and even the medical man, unless he be familiar with the true nature of the 'seizures' or fully alive to the history of the case, may be taken unawares, and feel so dubious about their purport and outcome as to be unable to give a reassuring prognosis.

And yet the seizures which I have in mind are all consistent with long life and with good health at other times. Those with the more local effects may simulate or suggest organic disease of the brain; those causing serious instability may also be wrongly attributed to cerebral vascular disease or cerebral tumour; those which cause pallor, *distress, disturbances of pulse-rate, praecordial* pain or discomfort and, more rarely, loss of consciousness, are apt to be ascribed to disease of the heart. We might reasonably include in this category ordinary faints or syncope and epileptic attacks, and Gowers [1], who did more to illumine this subject than any one else, discussed together under the broad heading of *The Borderland of Epilepsy*, syncope, vertigo, and certain other 'nerve storms' to be described.

Fainting and epilepsy, as being better known, I shall not consider here. The particular seizures which I wish to review include the aphasic, hemiplegic, and vertiginous varieties of migraine; vertigo whether due to labyrinthine disease or more transient vestibular disturbance; and the so-called vasovagal attacks of Gowers. If we except labyrin-

[1] *British Med. Journ.*, 1934, i. 89.

thine vertigo there is no demonstrable organic basis for any of these seizures. The physical overhaul between attacks, unless there be a coincidental pathology, gives a negative result. They are therefore placed in the category of the 'paroxysmal neuroses'. In the migrainous episodes temperament and heredity, sometimes with idiosyncrasy or allergy on the one hand, and transient disturbances of physiological equilibrium due to fatigue, worry, eyestrain, constipation, or mental stress on the other, may all play a determining part. To no inconsiderable extent the same influences play a part in increasing the liability to vertigo and vasovagal attacks. Anxiety of mind occasioned by the symptoms themselves, and the subsequent prostration when the storm is past, are apt to keep the patient in an unduly receptive state, and so prone to further storms.

It is my purpose to amplify a brief general account of these interesting, and by no means rare, neuroses with some case-histories illustrating their symptomatology, and justifying, as I think you will agree, their inclusion in the list of the 'alarming seizures'. Thereafter I shall shortly consider a few important principles in the management of cases.

Migraine and its Variants

If we are to study its less-frequent variants we should start with a clear image of the better-known phenomena of migraine. As commonly seen it is a disorder chiefly of the active period of adult life, affecting both sexes, depending strongly upon hereditary endowment, and showing a tendency, better marked in men than in women, to spontaneous remission after the age of 50. It is characterized by symptoms of very variable severity, and occurs in intermittent paroxysms separated by days, weeks, or months. The paroxysms come 'out of the blue', and often for no apparent reason; on the previous day the patient may have felt particularly well. They commonly start on waking in the morning. The first symptom may be a hemicranial brow ache, or more generalized headache, but before this there is often a passing disturbance of vision. Fortification spectrum or teichopsia on the one hand, or a blind patch or hemianopia

on the other, are the commoner forms of aura. The headache in a case of average severity becomes more intense during the day; sometimes it is completely crippling, and necessitates retirement to a quiet and darkened room. Nausea or repeated retching and bilious vomiting follow. The patient looks pale and ill, with dark rings under the eyes. Twelve hours is a usual duration for the attack, but it may be prolonged to twenty-four hours or, more rarely, through two or three days. There remains a sense of prostration, which takes another day or two to pass. Cold, fatigue, worry, eyestrain, train and motor journeys, and certain foodstuffs or beverages—notably rich or fried foods, chocolate, and eggs—are among the recognized precipitating causes. Mental workers who get little exercise are more prone to the disorder than others. The menstrual period and the menopause in women are particular times of aggravation.

Some patients escape with occasional attacks of hemianopia or teichopsia; some with slight headaches which cause little or no interruption to work; some experience the more familiar attacks at one time, and at another the aphasic, hemiplegic, or vertiginous variants which I am about to describe. There are also variants of another kind, in which abdominal symptoms predominate, whether as sickness, diarrhoea, or pain, or some combination of these with a general malaise, but always tending to a periodic or intermittent behaviour, and an equivalent duration of symptoms. Sometimes the abdominal manifestations are severe enough to suggest food poisoning or an abdominal emergency. In some cases there is a vague sense of soreness or discomfort about the liver region, and a look of sallowness almost approximating to icterus. Gall-bladders have been removed in cases of migraine misdiagnosed as cholecystitis. If a barium-meal examination is made during an attack of migraine or migrainous dyspepsia the stomach is found to be inert; it may take upwards of six hours to empty, and I have seen one case diagnosed as pyloric stenosis on this account.

In aphasic and hemiplegic migraine, usually on a basis of

the more typical ocular and hemicranial symptoms, there is superimposed a confusion of speech, the patient knowing well what he wants to say, but being unable to say it. With this there may be a sense of weakness in the arm, or sensations of numbness or tingling in the hand and lips and face of one side. More rarely there is motor weakness or even a transient paralysis. It can well be understood how 'strokes' are feared, or cerebral thromboses actually diagnosed in such cases. The symptoms, however, pass over quickly with the rest of the storm, and leave no relics behind them. Moreover, they can occur in subjects in whom it would be unreasonable, on the score of age, history, and physical findings, to suspect vascular disease, and there is often a personal or family history of indisputable migraine.

Vestibular or vertiginous migraine is characterized by attacks of profound giddiness, instability, collapse, and vomiting, indistinguishable in the main features of the attack from *Ménière's syndrome*, but separable (though often with difficulty) from the recurrent vertigo of labyrinthine disease by a history of previous migraine or associated migrainous phenomena, and by the absence of any evidence of aural disease such as deafness or tinnitus.

Aphasic and Hemiplegic Migraine

CASE 1. A young married woman, aged 31, of sensitive, intelligent type, was brought to me for attacks characterized by partial loss of vision, headache, numbness in the lips and one or other arm, and loss of speech. The headache was localized over one brow, and preceded the aphasia. During the attack she knew exactly what she wanted to say, but could not say it, and was aware that she was 'talking rubbish'. The attacks ended with vomiting, griping epigastric pain, and diarrhoea. They lasted for 4 to 6 hours, and were followed by prostration enduring for 2 or 3 days. They had caused her and her relatives the greatest alarm and anxiety. On one occasion when the left arm was numb she had no aphasia; there was well-marked aphasia on each occasion when the right arm was numb. She had other attacks of an abdominal type, which had at first been ascribed to 'food poisoning', and others with headache and giddiness. Constipation and nervous strain were particular determining factors.

CASE 2. A small, healthy-looking girl, aged 12, experienced 6 attacks in the course of 8 months, in which she complained of a feeling

of numbness and weakness 'all down one side'. Although she could move the arm she was quite unable to hold a cup. These symptoms would endure for about 10 minutes, and were followed by visual disturbance and a headache, which persisted throughout the day. In one attack she vomited. In all of them she 'went off her food', became drowsy, and for the next day or two was lacking in energy; her breath and tongue were unpleasant. Her mother had had 'terrible' periodic headaches throughout her life, and at odd intervals had experienced similar feelings in the arm, and on one occasion had dropped a teapot. A younger brother of the patient had 'acidosis' attacks.

The hemiplegic symptoms are usually, as in the first case, of a sensory kind, and referred to as weakness, numbness, or tingling, rather than as loss of power, but actual loss of power may occur as in the second case. Although slight paraesthesiae and transient dizziness were mentioned in other cases, I have encountered only six examples of aphasic and hemiplegic migraine, and the same number of vertiginous seizures among 213 migrainous patients. Probably the neurologists see a higher proportion of these interesting cases.

Vestibular Migraine

CASE 3. A man, aged 48, whose mother had suffered from bilious attacks, complained that since boyhood he had been liable to bilious attacks followed by extreme drowsiness. He was even at times found asleep by the roadside on the way home from his work. (Drowsiness is well recognized as an occasional manifestation of migraine.) Latterly these attacks had taken on a new form, and were characterized by severe vertigo with sickness, giving place to the old drowsiness with slight headache. These attacks would come on at any time, but especially in the morning. After them he felt completely 'washed out'. Cigars, a missed bowel movement, worry, and a stuffy room were recognized as determining causes. There was no evidence of ear disease.

CASE 4. A woman, aged 48, always 'highly strung', had been liable to sick headache at long intervals. In some of the attacks she was temporarily blind in one eye. Three months before seeing me she was overcome with giddiness one morning, 'everything went black', and she saw quivering specks of light. There was much nausea, and she did not feel really well for several days. A fortnight later she had a similar seizure, with a sensation of falling forward. Others followed, and were accompanied by severe headache, which left her scalp sore. Aggravating factors at this period of exacerbation included great domestic sorrows and anxieties, and a secondary anaemia.

We find, therefore, that the victims of what we may call 'ordinary migraine' may at times experience other types of seizure, characterized by aphasia, unilateral sensory or motor disturbances in the periphery, and vertigo. A careful unravelling of the history and an analysis of the symptoms in the particular attacks which have caused alarm will, however, nearly always reveal their true nature. A family history of migraine may provide the necessary clue. The vertiginous attacks clearly suggest Ménière's disease if insufficiently analysed. We may therefore conveniently pass here to a consideration of some other cases of vertigo of varied aetiology.

Vertigo

If we exclude intracranial disease and occasional causes such as wax or water in the ear, the pathologies underlying recurrent vertigo include: (*a*) the otosclerosis which occurs at or after middle-life, and accounts for the majority of cases; (*b*) chronic otitis media; (*c*) sudden accidents to the labyrinth—inflammatory or perhaps due to local haemorrhage; (*d*) vasomotor disturbances giving rise to abrupt fluctuations in the blood-pressure, in which group we may probably include the cases seeming to follow directly upon emotional stress; (*e*) tobacco excess; and (*f*) migraine.

The usual story of a major attack of vertigo is that of a middle-aged subject who has previously noticed a slight progressive deafness and frequent tinnitus in one ear, and is seized, at any time or place, whether in the street or in his bed, with violent giddiness, in which objects seem to revolve around him or the floor appears to rise to meet him. He is compelled to hold on to the nearest railings or to lie down, but this brings no relief to the sensations, which may continue for minutes or hours. Repeated vomiting may follow, and sometimes uncontrollable diarrhoea. There is great prostration and, more rarely, a feeling of impending dissolution as real as that which is recorded by sufferers from vasovagal attacks or occasionally in association with the angina pectoris of coronary disease. As in migraine, pallor, greyness, and coldness are noted by eyewitnesses. There are

usually intervals of days, weeks, or months between the major attacks. The patient is left shaken by them, lacking in confidence, depressed, unwilling to go out of doors, and not infrequently with a persisting sense of slight unsteadiness, which is worse in traffic or with sudden movements of the eyes or changes of posture. When deafness in the affected ear becomes complete the vertiginous seizures may become less frequent and sometimes depart never to return.

It is clear that the labyrinthine disease, although an essential conditioning factor, is not alone responsible for the attacks, for if this were so the vertigo would be continuous instead of transient and occasional. Of the causes predisposing to the attacks, states of general physical or psychological unfitness, such as result from the menopause, or from a too precipitate loss or gain in weight, fatigue, anaemia, and mental anxiety, are all noteworthy. The determining cause of the individual seizure is hard to trace, but an empty stomach, a sudden movement, or a strong emotion are among their number. Of perpetuating causes I believe the anxiety and apprehension engendered by the attacks themselves to be real and outstanding. After all, nothing could be better devised to provoke a nervous instability than attacks of genuine physical instability coming on without warning and beyond all voluntary control. A conditioning physical cause is also much more likely to be operative during states of nervous tension and unrest.

Case 5. A woman, aged 60, who had previously consulted me for other troubles of a minor kind, was seized, after a period of grave family worry, with a succession of vertiginous seizures, in which she was prostrate, vomited repeatedly, and experienced much singing in the ears, especially in the left ear. She did not sleep, she was terrified by the attacks, and apparently had feared a stroke. She had lost a stone in weight since her previous visit to me a year before. The only physical finding was deafness in the left ear. The entry in my notes was 'labyrinthine vertigo; aggravation by fatigue, loss of weight, constipation, and worry'.

Case 6. A man, aged 54, stated that he was well until 3 years previously, when something suddenly 'popped' in his left ear, and he had a severe attack of vertigo. He remained liable to attacks of giddiness thereafter, in which he had to grasp neighbouring objects for support.

The attacks were steadily diminishing in severity. His blood-pressure was 230–140. I have never convinced myself that hyperpiesia itself (apart from a vascular lesion) could cause true vertigo. In a long series of my cases of vertigo a normal or low blood-pressure was found to be more common than a high one. In this case, however, I surmise that the high blood-pressure may have been indirectly responsible by causing a local vascular accident.

CASE 7. A young man who had undergone a great deal of domestic strain for a number of years, lost his mother suddenly. On the day before the funeral, and again on the morning of the funeral, he awoke with nausea and intense giddiness, the fireplace appearing to revolve to the right. There were no physical signs of disease, and in this case no deafness or tinnitus, and there was no history of migraine or tobacco excess. He had always been able to make his right Eustachian tube 'click'. Here the evidence for an aural contribution was minimal, and I concluded that emotional stress was the predominant factor.

CASE 8. A professional man, aged 54, who had been under my care 4 years previously for a duodenal ulcer, came to see me much exercised about symptoms of quite another kind. For 6 months he had noticed increasing deafness in the right ear. One day he suddenly collapsed with intense giddiness and violent vomiting, and thought that he might die in the attack. He had to be carried home, and remained ill all day. Four other attacks followed in the next few weeks. He was greatly relieved in his mind by the reassurance given. Three months later he reported that deafness had become complete in the affected ear, and that he no longer had any giddiness.

I could recount the histories of many other cases of vertigo in which anxiety and apprehension were much in evidence, leading in some to a bedridden invalidism. Whatever other contributory measures or treatment are employed, I have again and again been impressed with the value of a simple explanation and a full reassurance. Disabuse your patient of all idea of 'strokes' or of cerebral or heart disease, and you will have given him a valuable helping hand. There is no specific medical treatment of the ear disease, and the cases suitable for treatment by the neurological surgeon must remain in a minority and be selected with the most exclusive care. There is the more reason, therefore, to concern ourselves with the associated factors in the management of these cases.

Vasovagal Attacks (Gowers's Syndrome)

I have mentioned the sense of impending death as an occasional symptom of vertigo. In vasovagal attacks (Gowers's syndrome) it is one of the most constant and quite the most urgent and dreaded of symptoms. These attacks affect adults of either sex and any age; they are more frequent in women than in men. In my experience the victims, almost without exception, have been affected simultaneously by a minor cause of general physical ill health and by some anxiety or mental stress. As with vertigo and fainting, but for an even more imperative reason, the anxiety engendered by the attacks themselves is a strong perpetuating factor. The attacks 'come out of the blue', and may last minutes, or half an hour, or for longer periods. They leave a sense of prostration afterwards. A visceral disturbance, such as vomiting or diarrhoea, a bowel wash-out, or an oesophageal or intestinal spasm has sometimes precipitated the seizure, but no such disturbance can be traced in the majority of cases.

The chief complaint is of 'a sense of dying'—*not* a fear of death, which is sometimes even desired, so intolerable is the distress of the attacks. I have sat by the bedside and been assured by a patient that this time the end had come. In other cases of a minor kind a sense of 'something dreadful about to happen', of 'fading away', of 'floating in space', or a peculiar 'sense of unreality' are described. There is a complaint of profound malaise, of coldness, sometimes of shivering or trembling, and of heaviness, immobility, or powerlessness in the limbs, and, in these circumstances, patients have told me that even if a cup of restorative were within reach they would be unable to lift a hand to take it to their lips. This immobility is strongly reminiscent of the frozen powerlessness observed in the rabbit 'fascinated' by the stoat or snake, and one patient, who had seen an animal in this state, was forcibly reminded of the incident by her own symptoms. Praecordial or substernal discomfort, or genuine pain spreading into the left side of the neck and down the left arm, or a sense of constriction in the chest is

common, and tingling in the finger-tips and sometimes true tetanic spasms are also described. To observers the patient looks very ill and pale, and may be cold to the touch. Even medical men have been deceived, and thought that death was imminent. The pulse may be rapid or very slow. In one case of mine it fell on occasion to 36 and once even to 19 to the minute. Sometimes the general symptoms, sometimes the cardiac symptoms, predominate, but the 'angor animi' is rarely absent. These attacks are often diagnosed erroneously as 'heart attacks'. Some of them do, indeed, closely simulate angina pectoris. Many of the so-called pseudo-anginas in women and younger subjects are examples of Gowers's syndrome. As a rule consciousness is retained, but occasionally it is lost, and when this occurs it is for much longer periods than in the case of an ordinary faint.

CASE 9. A young woman, previously healthy and placid, underwent an operation for appendicitis. During convalescence she developed almost every morning a pain across the abdomen, followed by a bowel action. On 10 or 12 occasions this was succeeded by tachycardia, feelings of deadness or numbness in both arms, especially in the left, generalized tremor, and a most acute sense of dying. She then recalled that she had twice experienced something similar before the appendicectomy. With reassurance and general treatment she quickly outgrew the attacks.

CASE 10. A medical man, aged 38, who was recently convalescent from a gastric haemorrhage and had experienced the sensations accompanying ordinary faintness, took a rather large dinner of eggs and spinach. This was followed by feelings of fullness. He then became faint, but in spite of lying flat on the ground the feelings grew worse. The attack lasted fully half an hour. There was no loss of consciousness. The patient thought he was dying, and so did his wife. 'He looked ghastly', and it was not unnaturally assumed that he had had a further haemorrhage. At the end of half an hour there was a shivering attack. I saw him a few minutes later, when he was warm again, but still very pale. His pulse-rate was 72 to 80; there was no haemorrhage.

In this case there was no praecordial distress. To the patient and medical friends who were present the episode was something different from an ordinary faint, a state in which angor animi is not described, and the symptoms are generally of short duration or quickly followed by loss of consciousness.

CASE 11. A woman, aged 51, of nervous temperament, and of the anaemic, flabby type, sent for her doctor urgently one night on account of epigastric and substernal pain. She thought she was going to die. She looked 'ashy' white, and had a very slow pulse; she recovered slowly, the whole episode lasting about one hour. She gave a confused account of previous attacks, some of which sounded dyspeptic, while in some she experienced praecordial and left arm pain as a result of effort or during a game of bridge. In these attacks she had a 'feeling in the throat and difficulty in drawing her breath'. She had a sharp aortic second sound. Her blood-pressure was 160–100. Many members of her family, including a sister, were reported to have died suddenly. The decision as between true angina pectoris and Gowers's syndrome was here a difficult one. Later she was re-examined, and on two occasions a normal electrocardiogram was obtained. She remained fairly well during the next year, except for 'indigestion', and experienced no pain or dyspnoea on walking. She was then seized with a severe attack of stomach pain while driving in a car, and was taken to a chemist's shop, but becoming worse was moved to a doctor's house. Here the doctor, seeing her for the first time, made a confident diagnosis of angina. I saw her shortly afterwards, and was much more in favour of Gowers's syndrome than before, and considered anaemia and anxiety again as underlying causes. Her blood-pressure was now 140–95. A little later her own doctor was called, on more than one occasion, to see her in attacks in which the sense of impending death was predominant, and pain quite a secondary symptom. There was now an additional complaint of 'stiffness in the hands and feet'. These attacks occurred at rest in bed, and were so unlike true angina that the alternative opinion was finally adopted, and treatment modified accordingly.

Further descriptions of vasovagal seizures are given in Chapter V.

It is noteworthy that the same sense of constriction in the chest and angor animi which these patients describe can occur in anaphylactic shock, and that they may also be evoked by too large a dose of adrenaline given hypodermically. In either case it seems reasonable to suggest that an abrupt fluctuation in the blood-pressure is an operative cause. In some cases vasovagal attacks, like migraine, occur at intervals throughout a long life, and although patients come to realize that they will survive them, the sense of dying or angor animi is not one whit diminished at the time. I have seen the fear and misery engendered by the attacks in women of frail constitution or hysterical type lead to

hed-ridden invalidism, but most patients continue to go about their affairs, and many, presumably, outgrow the attacks altogether, or experience them in diminishing degree.

The vasovagal attacks of Gowers are by no means as rare as they are sometimes supposed to be. I have collected 82 cases in the course of private practice, as compared with 72 of labyrinthine vertigo, and 213 of migraine (all types). They are commonly labelled as 'heart attacks', 'pseudo-angina', 'nerves', and 'anxiety attacks', but they are so true to type, in respect of both their subjective and their objective phenomena, that these varied and looser nomenclatures should not, in my belief, be sanctioned. They are at least as deserving of separate classification as fainting, epilepsy, migraine, and vertigo, with which they also bear definite relationships.

Summary

We find, then, that all of these seizures tend to occur in persons of particular type or temperament; they are paroxysmal and intermittent, 'coming out of the blue'; they are of limited duration; they are associated with, and leave in their train, no structural, nervous or visceral damage; they tend to create grave anxiety and apprehension; they are more likely to develop at times of general unfitness, whether of a physical or a mental kind; and, in no small degree, they seem to merge with one another and to possess common clinical features and aetiological characters. Just as migraine has relationships with epilepsy and may occasionally be replaced by an epileptic seizure, so also it may take on a vertiginous character and remind us of, or be mistaken for, labyrinthine vertigo. Labyrinthine vertigo in turn may be accompanied by the collapse and feeling of impending death which we have seen to be leading symptoms of the vasovagal attack. I have several case-histories of patients who were afflicted both with migraine and with vasovagal attacks. Bad bouts of migraine, vertigo, and vasovagal distress are all liable to be followed by feelings of prostration enduring for a day or more, and the two first are sometimes

followed by a profound sleep. The vasomotor phenomena of fainting—namely, coldness and pallor—are common to all three, and in all three loss of consciousness may very occasionally occur. Whatever the nature of the neuronic cyclone we find grounds for arguing that these various manifestations represent disturbances of a similar kind, but varying in degree and occurring at different levels in the sensorium.

Wilks [2] long ago remarked: 'It is undoubtedly true that there is not a single organic disease of the nervous system which may not be simulated by a functional and curable one.' Hemiplegic migraine has its counterpart in organic hemiplegia. The vertiginous episodes have their counterparts in cerebral and cerebellar disease. I have elsewhere given reasons for supposing that vasovagal attacks are expressive of a medullary storm, and the sense of impending death may actually occur with organic lesions which involve or embarrass the medulla oblongata [3, 4].

In the handling of cases in which fear and apprehension are an inevitable accompaniment it is clearly a grave error to suggest a diagnosis of organic disease, and yet, their true nature having passed unrecognized, it is by no means rare for vertigo and the stranger variants of migraine to be ascribed to cerebral disease and for vasovagal attacks to be called 'cardiac'. A general regulation of the patient's way of life, the discovery, and, so far as possible, the elimination of adverse physical or psychological influences, and the judicious employment of sedatives such as bromides and luminal to 'damp down' native irritability, play a reasonable part in treatment.

In migraine a strict exclusion of eggs, chocolate, and fats from the dietary is often rewarded. More exercise and a moderation of mental activities commonly help. But whatever measures we employ it is of the first importance to examine carefully, to explain simply, and to reassure fully, and so to remove, so far as may be, the crippling element of doubt or dread. In dealing with these cases we are repeatedly reminded that the study of the patient as a whole, and of his environment and his family history, by completing our diagnosis or 'thorough knowledge' of his malady, gives us

the surest guidance in our choice of measures for relief, whether these be of a physical or of a psychological kind. Even when ultimate pathologies remain obscure it is a matter for comfort that it lies within our power to recognize that some of the more alarming episodes of medical practice need not, in fact, occasion any fear of an unhappy ending.

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XXXII

OF NOSOPHOBIA

Few would deny that fear may become or engender disease. It might almost be described as the great pandemic malady. I have, alternatively, referred to it as one of the two great primary symptoms. Pain is the other one. They are, in fact, what our patients chiefly bring to us. Fear and anxiety (which may be regarded as low-grade continuing fear) are probably commoner symptoms even than pain although they remain more frequently unspoken. Fears and anxieties may be reasonable or unreasonable, but they do not lack a cause. They may be related to external circumstances, to domestic or economic difficulties, to bombs, or to the international situation. But they may be related also, and are probably more frequently related, to the patient's internal economy and his private thoughts about it; to his symptoms and their possible import; to the effects which illness or accident may have on prospects, activity or earning power; to ideas of pain and suffering and their tolerability; and to ideas of death and dying. Many of our patients, indeed the majority, who harbour fears or anxieties about themselves have no structural disease although they may have definite physical symptoms. Anxiety itself may be a main cause of these symptoms and is in turn aggravated by them. In such case Anxiety becomes, in fact, the diagnosis or the real disease. But we sometimes tend to forget that patients with organic maladies and injuries also harbour fears and apprehensions and then, because they show no outward signs of neurosis, their unspoken troubles (often of a degree and kind to retard progress or aggravate suffering) remain uncomforted.

The Meaning of Nosophobia

Among the twelve diagnoses which appear most frequently in my case-records Anxiety comes second on the list. In four of the other eleven, including the first on the list, it is probably an important causal or contributory

factor. But there is no disease, whether grave or trivial, in which fear may not sometimes play a part. Nosophobia is derived from the two Greek words *νόσος* meaning disease and *φόβος* meaning fear. It has come to be applied particularly to a morbid dread or neurotic fear of disease, but there is no reason why it should have this limited meaning and I shall here employ it in its widest sense. It can then be used to describe a fear of an existent or a non-existent disease, of a disease which a patient has or thinks he has or fears he may acquire, or of the consequences which disease or injury may bring to him or those dependent on him.

While allowing that there are phlegmatic, insensitive, and care-free individuals who make light of their physical disabilities we would do well to presume the presence of some degree of anxiety in nearly every general medical case reporting for diagnosis and advice; in most acute illnesses in which consciousness is not dimmed; in most bad surgical cases and accidents and woundings in which the mind is unclouded by the effects of shock and haemorrhage; in most cases of sudden bleeding before serious weakness supervenes; in most conditions calling for the knife, for here the fear of the operation and the anaesthetic aids and abets the fear occasioned by the illness; and in quite a large proportion of other conditions which to us seem very trivial. Can any of us say that we have submitted to gas for a dental extraction or the incision of a whitlow without a passing flicker of anxiety? Can any of us maintain that transient pains, discomforts, or rashes have never created apprehension in our thought?

By comforting explanation and reassurance, by minimizing fears when there is no reason for them to be otherwise than minimal, by abolishing uncertainties about organic illness in the minds both of patients and their relatives whenever possible, be the illness heart disease, pneumonia, phthisis, appendicitis, cancer, or measles, we can bring genuine and sometimes surprising benefits to the mind and to the body through the mind. By demonstrating and relieving the fear factor in the 'functional' case we can often remove or greatly benefit the disease itself. One has only to

recall facial expressions of relief or halting words of thanks or even sudden changes for the better, which are within the experience of every doctor, to feel sure that comfort of this kind, even if it is not always lasting, is an essential therapeutic contribution. The too-frequent omission of the encouraging word or the pat on the shoulder is not, let me insist, to be ascribed to hardness of heart or any callous attitude, but simply to a failure to realize that such gestures are needed or to a preoccupation with symptoms which seem so far physical as to call only for physical methods of treatment. Even in the resuscitation ward after an air-raid I have sometimes noticed two, three, or more people engaged on a fracture or a wound and giving it every care and attention, but without one of them pausing to spend a moment with the patient afterwards to tell him that 'It's not too bad, old chap', or 'We shall be able to save your limb', or to the chilled and frightened girl 'We'll soon have you warmed up and feeling better'. It takes no time and it means so much and, having escaped one terror, the poor things ought not to be allowed to suffer a moment of unnecessary dread. We become so familiar with the general appearances and course and prospects of common diseases and so interested in local pathologies that we tend to forget the minds and the prevailing ignorance in the minds of our patients, and also that many of them are too timid or incoherent to ask the very question that would give us the opening we need to set their hearts at rest. So many medical students develop fears of disease during their apprenticeship that it is curious that they should so readily overlook their influence or underestimate their prevalence in later life in others.

We should remember too the many agencies at work which foster a morbid interest in disease—the daily and still more the Sunday papers, the advertisements of patent medicines, the advice or gloomy talk of friends, the knowledge of the illnesses and deaths of relatives. Although in times of health these may be the pepper and salt of life for some gossiping folk, when sickness comes it is their smart which prevails rather than their condiment effect.

Types of Nosophobia

Let us now consider some of the more important varieties of this fear of disease, of the prevalence of which we need entertain no doubts.

(1) Nosophobia may, in accordance with the common usage of the *term*, take the form of a quite unreasoning fear of a particular disease from which the patient does not, in fact, suffer, or, alternatively, of an unreasoning fear that he may acquire it.

The *victims* of this form of the malady are usually endowed with psychoneurotic or psychotic personalities. Syphilophobia is a well-recognized example. It may afflict both those who have exposed themselves to a risk of infection and those who have never once incurred it. A sense of guilt dependent on faulty or puritanical upbringing may play a part in such cases. The anxiety tends to become fixed and magnified into a central obsession and may be extremely difficult to dislodge. Negative blood tests fail entirely to convince or satisfy the unhappy mind and serious mental derangement may follow. Phobias almost as resistant may be developed for cancer, but the majority of cancer phobias are of a much more manageable order and they do not involve feelings of taint or unworthiness.

(2) Another form of nosophobia is the dread of disease as a whole or of some common group of diseases such as the infectious or contagious group.

This tends to afflict nervous people with a smattering of knowledge about bacteria or the children of anxious parents who have compelled them to lead unduly sheltered lives. Medical students are often the temporary victims of disease phobias of this kind. They may lead to excessive washing of the hands or to misinterpretations of trivial symptoms which become so far magnified as to suggest one or more of the graver pathologies which find illustrations in the museum and the wards and about which the text-books are so graphic. These fears, too, are unreasonable. Although they may be said to have some foundation in experience they

remind us that a little knowledge can he a dangerous thing. They are usually quickly curahle hy a careful overhaul and a sensihle talk. It is not wise to laugh at them. A student came to see me some years ago convinced that he had a caneer of the rectum because he believed himself to he getting thin. He carried his own photograph ahout with him and frequently compared it with his face in the glass. I examined and reassured him thoroughly, reminding him that loss of weight in rectal carcinoma was only likely to develop in the later stages and to the tune of recognizable *symptoms* and *signs*, and finally appropriated his photograph. When last heard of he was hard at work in a husy practice and, let us hope, relieving other patients of their fears.

(3) A third and hy far the commonest form of nosophobia is that engendered hy more or less defined but unexplained physical symptoms.

Internal pains may suggest cancer in middle life. Pain in the right iliac fossa promotes fears of appendicitis, not only in patients, but also in their doctors, and has resulted in the removal of countless innocent organs, often enough for symptoms whose closer analysis would scarcely have been consistent with a local inflammatory lesion. Coughs and sweating and loss of weight suggest tuhercnlosis. Vertigo and aphasic migraine suggest strokes. A fear of going out of their minds is common in the psychoneurotics. Fainting suggests heart disease, of which it is, in fact, very rarely a symptom. The vasovagal attacks of Gowers suggest angina pectoris or heart failure with particular aggravation hy the strange physical sense of dying which may accompany them. In all such cases a confident diagnosis and explanation are the first contribution to treatment whatever other measures may he employed to combat the whole disorder or to correct an emotional situation. These phobias are more reasonahle. They are hased upon a wrong interpretation of symptoms, it is true, hut often of symptoms which have taken time to unravel and may have provided the medical profession with diffi-

culties and indecisions which do not escape the notice of the intelligent patient.

(4) Nosophobia can often be traced to misconceptions for which the doctor is to blame, to erroneous or incomplete diagnoses, to a simple failure on his part to explain and reassure because he had not appreciated the patient's state of ignorance or apprehension, or to a needlessly gloomy or guarded prognosis, or to forgetting to give a prognosis at all.

Fears encouraged by omissions in this way are by no means rare. Other fears may originate in the unguarded public pronouncements of medical men which must then be accounted sins of commission. Whenever possible we should tell our patients that they are going to get better, or, at least, that they are doing well, or, even when we are dubious about the issue, that they are fighting a good fight and that everyone is out to help them. Those physicians and surgeons have always been the most successful who have best inspired hope and courage in the sick-room.

(5) Finally, with the fear of disease and its pains and penalties, we must couple the particular fear of death which illness cannot fail, in certain circumstances, to promote.

Busy with the management of a case and with our own anxieties it is strangely easy to omit the necessary word of encouragement to a victim of sudden haemorrhage or other urgent symptoms, although the whole atmosphere of the sick-room and the expressions on friendly faces unable to conceal care, not to mention the disturbing symptoms themselves, must appear as danger signals. Oxygen cylinders should be kept out of view when not in use, for oxygen, quite wrongly, suggests only desperate situations to the lay mind. Curiously enough the terrible feeling (*not* fear) of impending death which is experienced by the victims of vasovagal attacks and vertiginous seizures and anaphylactic episodes and in some cases of angina pectoris (the angor animi of the older physicians) is rarely, if

ever, encountered in those whose lives are immediately in jeopardy.

Let us pass now to some case-histories illustrative of these various types of fear.

CASE 1. *Syphilophobia.* A man, aged 35, who had been a prisoner in German hands during the 1914–18 war for four years, was treated during that period for a urethritis, but denied exposure. After his return he was pronounced free from infection and his W.R. was also negative. In the course of the next few years he had much sorrow and loss, his first wife dying in childbirth and his second from a cerebral abscess. A year before I saw him his urethral discharge reappeared. He was treated without a bacteriological examination. My notes state that 'he has developed a persistent obsession that he has syphilis. He complains of pains in the sacrum, the perineum, the neck, the eyes, and under the finger nails, of flatulence and insomnia and has lost a stone in weight.' I discovered a to-and-fro aortic murmur, which was rather disconcerting, refrained from discussing it with him, and admitted him to hospital for further investigation with a reassuring forecast. There we obtained another negative blood W.R. and also a negative urethral smear, and, better still, a history of three attacks of rheumatic fever in boyhood. He was at the time much comforted by these reports and a vigorous reassurance, but I have not heard how he fared subsequently. The background of a long imprisonment and his domestic tragedies probably played a large part in maintaining his anxiety of mind and conditioning the phobia into which it had crystallized.

CASE 2. *Syphilophobia.* A nervous Jew, aged 31, married and with children, developed warts on the hands and a friend told him that they were venereal. He was terrified and began to be physically 'sick with worry'. Pains in the joints followed and then he thought he had a stricture. He lost energy and all interest in his business and dropped two stone in weight. An opportunity of dealing with his friend would have been welcome.

CASE 3. *Infection phobia.* Many of us must have had transitory fears of septic or venereal infection from patients during our student days or afterwards. One contemporary of mine, now dead of a disease which he never feared, developed what amounted to a compulsion *neurosis in regard to the possibility of infection. Having washed* in the hospital he would wash again in the students' club before his meals, open the swing doors with his elbows, eat his College lunch, and then flame the end of his cigarette before putting it in his mouth. The unhygienic condition of the kitchens and dining-hall in those days and the fact that the food and the utensils must have passed through many unwashed hands before it reached him did not seem to worry

him. The fact that hundreds of men risked dining in College year after year and took none of his precautions and yet acquired no fell disease also failed to impress him. His nosophobia was distinctly unreasonable.

Case 4. *Illness and fear engendered by knowledge of disease in others.* In the course of one morning's out-patients recently we had two patients with symptoms resulting from this cause. One was a healthy girl of 18, about whose heart some anxieties had been entertained in childhood, although she then had no symptoms. She had recently complained of momentary stabbing pains in the sub-mammary region which did not at all suggest cardiac disease and the examination was negative. Her mother then told us that the girl had been working for a lady with heart disease. The association of a past suspicion of cardiac trouble and the spectacle of real trouble in another provided the mental basis for the symptoms. The other patient was a young married woman complaining of loss of weight, sweats, dry mouth, and multiple bodily pains, but without attendant objective signs of disease. She freely admitted on questioning that her symptoms had all dated from the loss of a friend from pulmonary tuberculosis and that she was living in dread of this disease.

Case 5. *Nosophobia due to indiscreet pronouncements by medical men.* I was once consulted by two old spinster sisters who arrived in a great state of trepidation. A distinguished surgeon had given it as his opinion that a diet consisting largely of vegetable foods and carrots would protect against cancer. They had embarked upon his programme, but it had suddenly occurred to them that they might have started it too late in life and that the seeds of cancer might have already gained a foothold! It is not easy to eradicate a disease phobia when it has been prompted by a man supposed by the public to be vested with high scientific authority. Let us hope, nevertheless, that I was successful both in relieving their minds and assuring them that their tedious diet was not really necessary.

Cancer Phobia

Apart from its high mortality and, in many cases, its relentlessness, cancer has inspired fear in the lay mind *because of its supposedly inevitable association with grave* pain. We would do our patients and the public a real service if we were to remind them more often, firstly, that cancer in its early stages is becoming gradually more eradicable and, secondly, that it is by no means always a painful disease; that carcinoma of the stomach, the liver, and the bowel, for instance, can all run a painless course (although we know

they do not always do so), and that when the disease is incurable and accompanied by pain a great deal can be done to relieve that pain. There are deaths more miserable than many of the cancer deaths which are not a source of public dread—deaths, for instance, from slowly progressive central nervous disease with loss of speech, power, and sphincter control.

In the presence of cancer we are always faced with the problem of whether to tell the patient the diagnosis. No hard and fast rule can be made. Sensitive elderly folk whose days are short can often be spared the knowledge. Sensitive younger folk, women especially, are better spared it in many cases. Many never ask us for a diagnosis and yet leave us suspecting that they knew it all along. Men with responsibilities and other brave people, both religious and agnostic, prefer to be told, and it may be our hard duty to decide for ourselves from what we know of them that this would, in fact, be their preference; they are then, with our help, in a position to gather their cloak of courage round them and to set their affairs in order. When we decide not to tell dissimulation may not always be easy, but in the case of gastric and colonic cancer it is always legitimate and not untruthful to speak of 'a severe ulceration' of a type suitable or unsuitable, as the case may be, for operative treatment. Some patients and especially women with breast cancers, will conceal their disease until it is far advanced rather than be told what they dread at a stage when it is amenable to treatment. Such psychological peculiarities *are puzzling, but in the individual case must be viewed with* tolerance.

Cancer phobia without cancer is, however, far commoner than cancer phobia with cancer. I have carefully perused the notes of thirty-one cases in which cancer phobia (without cancer) was the main diagnosis. These are a mere fraction of the patients seen who barboured the fear in some degree. There were twenty-one women and ten men. The average age was 50, the youngest 33 and the oldest 75. Thirteen were described as nervous, very nervous, or as having had a nervous breakdown on one or more occasions. The physical symp-

toms complained of were generally of a kind associated with emotional disorder. Thus, fourteen, with or without a specific mention of neurosis, were the victims of spastic colon or other colonic discomforts, of flatulence, globus or rectal spasm, or had had an abdominal exploration. Two patients had duodenal ulcers, and two cholecystitis. One had hyperpiesia.

In six cases, all women, there was a mention of sore or dry tongue or mouth or of altered taste with no evidence of a local cause for the symptoms. In such cases I have come to expect or inquire for a cancer phobia. Is the condition perhaps related to the dry mouth of more acute anxiety? One case was cured of the symptom and her fears by the interview and another greatly relieved by the assurance given.

Twelve patients in the series had lost a near relative or friend or neighbour from cancer or had intimate knowledge of a case or cases. Two were in the habit of reading articles in the papers or other literature bearing on cancer.

CASE 6. A very intelligent middle-aged layman, with expert knowledge of hospital administration, developed a troublesome lumbo-sacral pain after a blow in the back. On a basis of his medical half-knowledge and a vivid imagination, his age, the persistence of his symptom, and a contrast of his present state with his normally good health, he built up an association which seemed to support his fear of cancer. He slept badly and lost a stone in weight. He saw several doctors. He was cured by a single explanation and reassurance. Two years later he was seen for a much slighter anxiety about his heart and again relieved. Later he developed a duodenal ulcer which caused him no serious anxiety and responded to orthodox medical treatment.

CASE 7. A spinster, aged 70, had twice been treated successfully for rodent ulcers. Her brother had died of cancer of the gullet. Her friends told her that she was getting thin. She had lost a stone in weight, but had taken four years to do so. She was given to reading literature about cancer. There were thus several good causes for her fears.

CASE 8. A married woman, aged 61, suddenly developed a bitter taste in her mouth and later cold feelings in the body and slight pains in neck and shoulders. She worried more and more about these symptoms and slept badly. Two distant relatives had recently died

of cancer. She had seen a doctor, but had not been given a complete overhaul or a reassurance of the kind she needed. Eight months later her daughter reported that she had been well from the day of the consultation.

Case 9. A nervous unmarried woman, aged 47, and passing through the climacteric, had twice had a nervous breakdown in earlier life. Her mother and paternal grandfather had died of cancer. Two months previously she had begun to worry and to sleep badly because a friend of hers was dying of cancer. Her symptoms included pains in the throat, rectum, and vagina. Three years previously she had had n disease phobia in association with abdominal symptoms.

It will be seen from these histories that the fears which we unearth in our patients nre often hy no means unreasonable and that multiple factors are often at work. We do unwisely to blame solitary causes for most of the neuroses, for other conditioning causes often conspire with what we would like to regard as the prime or central cause. A knowledge of the age incidence of cancer and of cases in the family, operating in conjunction with a phase of depressed health and an adverse comment of a friend upon our looks, might surely activate the imagination in any one of us.

The Need for Saner Education

Passing now to some general considerations, we may observe that the disease phobias are on the whole rarer in the simple folk of the working classes or the country-side than they are among the more sophisticated, the idler well-to-do, the more educated, and the office workers. The spread of information to-day is not all beneficial nor is it synonymous with a spread of knowledge. Much of the information is incomplete or ill-digested. Especially is this so in the realms of human anatomy, physiology, and pathology. Half-knowledge is always more productive of fears and superstitions than fuller understanding. More than one patient has consulted me for an upper abdominal tumour having for the first time discovered his ensiform cartilage!

Anxious parents dread acute infections and tuberculosis for their children and bring them up in an over-protected atmosphere, to their physical and psychological detriment. Occasionally we meet with quite young children who have

5. In the case of patients with visceral or other symptoms which we believe to be due to emotional causes, we should explain how fear, anxiety, care, and worry can themselves be the cause of such symptoms or at least serve as a contributory or perpetuating factor.

6. We are seldom justified in telling a patient that 'there is nothing the matter' but often in saying 'there is no organic disease'. Nor should we describe a disease as 'only nerves'. Such phrases do not convince because they are both unpopular and untrue. They express, furthermore, our own failure to explain things to ourselves in a rational or physiological way, and also our failure to get behind the curtain of our patients' minds.

7. Sometimes in suspected heart disease, mental disease, or cancer it may be necessary to avoid asking questions about the family history, or to seek the information elsewhere. It cannot help a patient with anginal symptoms to recall that several of his forebears died suddenly or a victim of a depression to recollect that an uncle and a cousin committed suicide.

8. Even in the case of the gravest disease and even when the patient knows its gravity, much can be done to lessen apprehension, to foster courage and to comfort distress by our expressed willingness to help and to go on doing all we can to discover the best means of help.

9. Kindness and hopefulness are immeasurable assets. I have not met such a contradiction in ideas as a positively unkind doctor, although I have known some who lacked gentleness of touch, or manner, or were handicapped by bad tempers. I have, however, met some who were too pessimistic, or too silent, who were careful enough in their methods of examination and physical treatments, and yet failed to meet their patients with insight and understanding and thereby failed to help them as much as they might have done in their essential task as comforters.

Looking back on personal experience and its slowly garnered lessons one is conscious of many opportunities lost, of judgements gone astray, of faults both of commission and omission, but one is also conscious, as we must all one

XXXIII

OBSERVATIONS ON THE ABDOMINAL AND CIRCULATORY PHENOMENA OF ALLERGY[1]

In recent times attempts have been made to spread the net of allergy too widely. Conditions having no clinical or aetiological relationships with the accepted allergic disorders have been discussed as possible or probable examples of these disorders. It is a primary duty of clinical study to define disease, to render descriptions more precise, and to establish diagnostic criteria. At present we include among the allergic disorders asthma, hay-fever, spasmodic rhinorrhoea, intermittent hydrarthrosis, urticaria, angio-neurotic oedema, and eczema. With regard to migraine and epilepsy, although they appear not infrequently in persons and families subject to allergy and the former may be associated with food idiosyncrasies, opinion is less secure. A paroxysmal neurosis, although it consorts with 'nervous' constitutions and develops in response to minimal stimuli, need not necessarily depend upon that type of idiosyncrasy which allergy implies. Activation of symptoms by anxiety or an east wind would not at present be considered as evidence of allergy. Certain gastro-intestinal disorders and circulatory phenomena have also been classified as allergic, but they stand in need of more careful portraiture.

It is the purpose of this paper to identify and define certain abdominal syndromes and circulatory disturbances which may be reasonably regarded as expressions of the allergic state and, on a purely clinical basis, to suggest criteria without which we should be unwilling to accept them as genuinely allergic.

Allergy and Anaphylaxis

The word allergy has not found its way into the *Shorter Oxford Dictionary*. In *Dorland's Medical Dictionary* it is

[1] *Lancet*, 1935, i. 1257.

described as 'a condition of altered susceptibility which causes an individual to react to a second inoculation of an antigen in a manner different from his reaction to the first inoculation (Pirquet). The term is now used to denote the natural hypersensitiveness of an individual as contrasted with anaphylaxis, which is hypersensitiveness artificially induced by inoculation.' The clinical relationships of anaphylaxis and allergy are, however, very close. Identical symptoms occur in the artificially induced and the spontaneously developed disorder. Main distinctions between the two conditions are that anaphylaxis depends upon a specific sensitization and has a limited course, whereas in allergic states precise specificity is rare or other forms of sensitiveness become superimposed upon an original form, while nervous reproduction of symptoms is readily conditioned. Cases of pure horse-asthma, for instance, are exceptional and in most asthmatics there is a multiplicity of circumstances which may condition or predispose to the attack. Furthermore, the clinical course of an allergic disorder is recurrent and unlimited.

It would also seem that anaphylactic symptoms, although more readily induced in persons subject to allergic disorders, can be produced in some degree independently of particular constitutional predisposition. Allergy, on the other hand, is expressive of an inborn or constitutional predisposition and for this reason can result from smaller and often infinitesimal or undiscoverable stimuli.

'*Experimental Disease*' *in Humans*

While serum-sickness is common, opportunities of studying anaphylactic shock in man are fortunately rare. It may baffle observation by proving immediately fatal. Some years ago, in conjunction with J. Fawcett, I wrote a paper entitled 'Cases of Delayed and Immediate Anaphylactic Shock with a note on the Circulatory Phenomena'.[1] I reproduce our descriptions and discussion of two cases here, together with an account of one other case seen since, for the sole purpose of portraying the 'experimental disease'

[1] *Lancet*, 1923, i. 825.

(which includes both serum-sickness and serum-shock), and considering thereafter how far it is possible to discover parallel phenomena in a group of 'spontaneous' cases which I have since, after careful consideration, classified in my files under the heading of allergy.

Case 1. *Delayed Anaphylactic Shock.* A young woman, aged 23, was admitted into Guy's Hospital, under the care of Mr. F. J. Steward, on 5 November 1922, with a 'septic' finger. Operations were performed on the 6th, 8th, 10th, and 12th, for spread of infection, amputation of the finger finally becoming necessary. On 10 November 50 c.cm. of antistreptococcal serum were given subcutaneously at the time of the operation. Four days later patches of urticaria began to appear, and there was slight evening pyrexia. The local condition after the 12th progressed satisfactorily. At 4.30 a.m. on the 19th, 8 days after the serum was given, the patient was wakened by breathlessness. She was seen at 5 a.m. by one of us (J. A. R.) and was then sitting up in bed with 'asthmatic' breathing. The respiration-rate was 30 per minute, expiration was prolonged and wheezing, and she was expectorating small quantities of clear mucoid sputum. Sibilant expiratory rhonchi were audible all over the chest. She was pale, and the pulse-rate was between 110 and 120 per minute. Urticaria was appearing in large patches all over the trunk and limbs; the lips, ears, and eyelids were swollen. The house surgeon, Mr. J. K. Milward, had given her an injection of liquor adrenalin. 1–1000 ℥ 2. Within 20 minutes the asthmatic attack was over, but she felt cold and shivery, the pulse remained quick, and urticaria continued to appear. She was packed round with hot blankets and bottles, and given hot tea and lactose. She was seen again at 8 a.m. By this time there were no asthmatic symptoms, but urticaria was still troublesome; she had vomited twice, had two actions of the bowels, and was completely pulseless. She complained of feeling 'washed out', but apart from the cutaneous irritation and swelling of the gums, made no other specific complaint; she was mentally alert, and quite rational and calm, although she had before been considerably perturbed by the respiratory distress. At 10 a.m. we saw her together; no pulsation could be detected at the wrist or ankle, or in the carotid or subclavian arteries. The heart was not then, or at any subsequent observation, perceptibly enlarged, and there were no murmurs. The impulse was readily felt, the rate was 120–140 per minute, and the sounds were of good quality. She was not cyanosed. She was warm and the temperature was rising. The capillary tide in the nail-bed was good. The question of further administration of adrenalin was discussed, but we were agreed that, with such a degree of tachycardia, and no such urgent indication as 'asthma' now persisting, it would be wiser to avoid the possible overstress to the heart which

a sudden rise in blood-pressure might entail. In spite of her apparently alarming condition a good prognosis was given, partly on the general impression of the patient's demeanour, the rising temperature, and disappearance of the shiveriness of which she had at first complained, and partly on the experience of the case referred to below. For more than 12 hours no pulse could be felt at the wrist. After 24 hours the radial pulse still could not be detected with certainty. Vomiting ceased, but the patient had some nausea and felt that she could not take fluids, except in the smallest quantities, for fear that she would be sick. She was pale and thirsty, had a moist clean tongue, and continued to state that she felt 'washed out' and intolerably tired, but that she found difficulty in getting to sleep.

She was treated throughout with warmth, small quantities of fluid, brandy and lactose by the mouth, and 6-hourly rectal administrations of 1 pint of 6 per cent. glucose. The foot of the bed was raised for a few hours, until she complained of the discomfort of the position. Sleep was secured at night with the aid of an opiate. Twenty-eight hours after the onset of the attack the radial pulse could be felt as a doubtful flicker, but not accurately counted. At the cardiac apex the rate could be readily determined as 120 to 130 per minute, but the sounds were not so clear as on the previous day. She now complained of acute pain in nearly all her joints. She could not open her mouth wide on account of pain in the temporo-mandibular joints, and the knees, ankles, wrists, and interphalangeal joints were similarly involved. There was no further trouble with urticaria. Aspirin was added to the rectal injections.

Almost abruptly at about 3 p.m. on the 19th, or about 34 hours after the first appearance of urgent symptoms, the pulse became quite good in volume and slower in rate, and from then onwards it improved steadily. By midday on the 20th the pulse-rate was recorded as 80 per minute. After a further 48 hours all the joint pains had disappeared, but there was complaint of some deep-seated pain in the muscles of the left thigh. After this her progress was uninterrupted, except for the development of a small patch of erythema below the left knee, and later of an abscess in the right buttock. On the morning of the 18th, when the 'shock' symptoms were at their height, the temperature reached 102°, but quickly fell again to normal. It rose during the period of the gluteal abscess, and became stable again after its drainage.

The remarkable feature of this case was the late development of severe shock-like symptoms, true anaphylactic shock being usually considered as an immediate rather than a remote phenomenon. Regarding serum-sickness as the usual anaphlyactic response in human subjects, this case might alternatively be viewed as an extreme exaggeration

of this response, for the symptoms of 'serum-shock' and 'serum-sickness' were coincident. Indeed the case suggests the essential unity of the two conditions. The early development of urticaria on the fourth day was perhaps an indication of hypersensitiveness. The patient was not an asthmatic subject, and there was nothing else in her history to indicate that she was previously sensitive to foreign proteins. She had at the time no recollection of ever having had serum before, but it was later elicited from her mother that she had had diphtheria nineteen years previously, and that she was given antitoxin at the time. As there was no history of alarming symptoms on this occasion it would seem proper to regard her illness as a genuine instance of sensitization by a previous dose. We thought it possible that immediate shock might have been averted by reason of the fact that she was under an anaesthetic at the time of administration of the serum. We were informed by Sir (then Dr.) P. P. Laidlaw that, although anaesthesia may relieve or avert bronchial spasm and so save life in the anaphylactic guinea-pig, it has little effect on similarly induced circulatory shock in dogs.

Case 2. *Immediate anaphylactic shock.*—In October 1918 a soldier was admitted to a main dressing station with a small wound of the buttock. He was pale, cold, and pulseless; he was vomiting and complaining of abdominal pains. So ill did he appear that special examinations were made to ascertain whether he might have an intra-abdominal lesion with haemorrhage. The wound was carefully probed and found to be quite superficial. He was not aware of having sustained any other injury. Abdominal examination was negative. Within a short while urticaria appeared and anaphylactic shock could be confidently diagnosed. The man had during his period of service received two previous prophylactic injections of A.T.S., after one of which he admitted to having 'felt bad'. He was examined probably within an hour or less of receiving the third dose of A.T.S., which had been given the same evening at an advanced dressing station. Mentally he was perfectly clear. He was treated as an ordinary case of surgical shock by warmth, elevation of the feet, and frequent small sips of fluid, but as after 2 or 3 hours the pulse was still impalpable he was sent down to a casualty clearing station with a special note. He there came under the observation of Major G. T. Mullally, who later reported that the man had remained pulseless for some hours, but was fit for evacuation to the base on the follow-

ing day. Asthmatic symptoms were absent, and gastro-intestinal symptoms were the most prominent apart from those of circulatory failure.

The symptoms in both of the cases described suggested a profound fall in the systemic blood-pressure of exceptionally long duration. Presumably the main volume of the blood must have accumulated in the splanchnic area. The absence of oedema and cyanosis, the rapid recovery and maintenance of superficial warmth, and the presence of a good capillary tide in the nail-bed would seem to exclude a capillary stagnation or heart failure. There was no unusual loss of fluid by sweating, diarrhoea, or diuresis, and the fluid intake was well maintained. The symptoms of circulatory shock persisted long after the disappearance of the bronchial, cutaneous, and gastro-intestinal reactions.

Neither before nor since have I seen any other condition in which the state of pulselessness manifest in these two cases, and persisting for so many hours, was consistent with recovery.

CASE 3. *Delayed anaphylactic shock.*—A young married woman was operated on for acute appendicitis at 7 p.m. on 17 November 1932. At the conclusion of the operation she was given an injection of anti-gas-gangrene serum. On the morning of 23 November I was called urgently to see her with Dr. C. H. Atkinson. After a short period of malaise she had abruptly developed acute anaphylactic symptoms, including generalized urticaria, great oedema of the lips and eyelids, sensations of constriction in the throat, with attendant alarm, profound pallor, and pulselessness. An injection of liq. adrenalin. 1–1000 ℥ 3 was given immediately and repeated later. In a few minutes there was a rapid improvement and visible subsidence of the facial oedema; the radial pulse, although quick and small, became palpable; the sensation of constriction departed. Vomiting, diarrhoea, and pyrexia followed with much malaise and some fever. In the evening there was still great irritation from the urticaria, but the case gave no further anxiety. *It was later discovered that this patient had been* given diphtheria antitoxin in childhood and that she had a bad rash. She has since shown herself liable to primula rashes.

It should again be noted that this patient received her second dose of serum while under an anaesthetic. A few years ago I had under my care a very anaemic patient, who

had twice displayed violent and alarming immediate anaphylactic reactions following blood-transfusion, but whose response to a further transfusion, purposely given under anaesthesia, passed without anxiety.

On the experience of the three cases described the circulatory phenomena of anaphylaxis may be held to include pallor, tachycardia, initial coldness of the surface and extremities, and pulselessness due to a profound and sustained fall in blood-pressure. In ordinary serum sickness a pulse-rate of 120 per minute is common. From the same cases we may also conclude that vomiting, purging, and diffuse pain are the outstanding abdominal symptoms of the anaphylactic state in man. Asthma, urticaria, 'angioneurotic' oedema, pyrexia, and multiple arthritis are among the other recorded symptoms.

Disturbances Arising Without Apparent Cause

Let us now see how far these manifestations find a parallel (*a*) in acute and anxious disturbances arising spontaneously, or (more correctly) without apparent cause, and (*b*) in certain chronic or recurring disorders of less dramatic character.

Case 4. *Abdominal allergic attacks; severe type.*—A married woman, aged 64, was brought to me by Mr. Hastings Gilford on 30 December 1931. Except for malaria many years previously her life had been healthy. *Her daughter suffered from asthma.* A year previously she had had an unexplained attack of malaise and sickness while abroad. In November 1930 she had had a sudden severe attack of epigastric pain and cholecystitis was suspected. In January 1931 she had an attack of quite a different kind, with violent generalized abdominal pain, vomiting, diarrhoea, and much shock. The vomitus was slightly streaked with blood. A succession of similar attacks followed at 2 to 4 weeks' interval. There were as many as 4 attacks within one period of a fortnight. An extreme degree of shock-like collapse was evident both to the patient and to others around her. The acute phase was generally over within 12 hours. The X-ray appearances of the gall-bladder were normal. She felt perfectly well between the attacks. A Chinese spiritualist, who affected to be able to see what was happening in the stomach, told her that she did not digest eggs! Most of the attacks had started at 2 a.m. *In one of the attacks her lips became tremendously swollen with angio-neurotic oedema.* In most

of them her tongue was raw and red and her lips tended to peel afterwards. I could find no signs of organic disease.

CASE 5. *Abdominal allergic attacks; severe type.*—A medical man, aged 54, consulted me for the attacks to be described below. He had had malaria and pneumonia in childhood. *One brother had had hay-fever.* Since childhood he had been liable to repeated abdominal attacks for which he had consulted many physicians. His longest free period had been 9 months, his shortest 10 days. The attacks generally started abruptly after premonitory lassitude. Fasting was a predisposing factor. In the attacks he had very severe generalized abdominal pain, starting under the rib margins, and of crescendo type. Nausea sometimes preceded, sometimes succeeded the onset of pain. Vomiting followed, and if it came early the attack passed more quickly. He was unable to eat or drink during the attacks, which would last from 24 to 48 hours. Throughout the attack he looked extremely pale and ill, and the pulse-rate rose to 120. He had a slight inguinal hernia, and during the attack 'the sac seemed to fill with fluid', which he could press back into the abdomen. The abdomen was slightly swollen and it hurt him to take a deep breath. He had given up pork and bacon because one attack followed a pork pie, and mushrooms and fish because his skin had shown a slight reaction to these, but without benefit. In one attack a surgeon was called to see if he had appendicitis. Between the attacks he felt perfectly well. He had had *hay-fever* for 30 years, and for 12 years at intervals he had been subject to *angio-neurotic oedema* of his hand, arm, and perineum, and on five occasions of the palate and uvula, for which he had entered a nursing-home, fearing that tracheotomy might become necessary. Excepting for a right inguinal hernia and a myotonic right pupil, first noticed 30 years previously, there were no signs of any organic disease.

In both of these cases we find gastro-intestinal and circulatory phenomena closely comparable with those shown by the patients with anaphylaxis, and including shock, pallor, tachycardia, vomiting, diarrhoea, and abdominal pain. In addition we have, as confirmatory evidence, simultaneous or associated angio-neurotic oedema in both cases, hay-fever in one, and a solitary relative with an allergic disorder in both cases.

Before reviewing the less dramatic but more frequent allergic dyspepsias (in which circulatory manifestations are lacking or inconspicuous) there are further points in connexion with the vasomotor phenomena of anaphylaxis and allergy which will bear consideration. Together with the objective pulse and blood-pressure disturbances of acute

anaphylaxis from serum there may be associated the 'sense of impending death' which, in conjunction with striking vasomotor symptoms, is so pronounced a feature of vasovagal attacks (Gowers's syndrome). Vasovagal attacks chiefly affect patients who are at the same time physically unfit and in a state of anxiety. There is also, however, an occasional association between vasovagal attacks and migraine, asthma, epilepsy, spastic colon, and angio-neurotic oedema. All in fact proclaim an inborn hypersensitiveness which may be expressed in one or more of these several ways. It is rare in any of these to discover a specific sensitiveness as a basis for the vasovagal episodes, but an occasional case may develop symptoms in the first instance in response to a specific cause.

Case 6. *Vasovagal attacks following a second dose of serum.*—A young man, aged 21 (a patient of Dr. A. W. Walters), whose feeding in infancy had caused much trouble and who had suffered from 'mucous disease' until the age of 7, was thereafter fairly healthy until the age of 18. He then sustained a concussion and fractured a leg in a motor-cycle accident, and was given tetanus antitoxin. At the age of 21 he was involved in another motor-cycle accident, was again concussed, and fractured a small bone in his left hand, and was again given antitoxin. After this he was very unfit with urticaria and pyrexia, and developed attacks in which he was suddenly seized with a feeling of impending death and uncomfortable sensations about his heart. These attacks would last from ½ to 1 hour. When he sought to change his position things seemed to 'black out' and he felt 'wobbly' at the knees. He was terribly scared by these attacks, notwithstanding that he knew little of physical fear, was a keen rider to hounds, a member of the Auxiliary Air Force, and, as his history *suggests, a none too cautious motor-cyclist.*

The attacks continued for a time after the phase of serum-sickness. His father had experienced similar attacks at the age of 27 but had outgrown them. I have no notes as to his appearance during these attacks but the subjective phenomena were those of Gowers's syndrome, of which the usual objective manifestations are pallor, coldness, and striking pulse and blood-pressure fluctuations. Had he experienced a solitary attack with urticaria immediately after the serum we should have accepted it as typical of anaphylaxis. It is reasonable to argue that the succession of attacks in this instance was initiated by a second dose of serum. The infantile and family histories suggest the conjunction with the therapeutic 'experiment' of an appropriate 'constitution'.

Allergic Dyspepsias

It is not uncommon to meet persons who are aware of a food-idiosyncrasy. Shell-fish and eggs, especially ducks' eggs, are well-known offenders and may give rise to gastric disturbances and erythematous or urticarial rashes. More rarely chocolate or coffee is blamed. Idiosyncrasies for drugs, not excluding those in common use like morphine (which may cause vomiting and collapse), are well recognized. The victims of these idiosyncrasies, however, although (like the horse-asthmatic) they exemplify a specific sensitiveness, usually have the sense to avoid what is poisonous to them and are rather less likely to consult us for recurring allergic disturbances than those whose sensitiveness lacks discoverable specificity. Of this latter group, I have selected a few examples from my files. The case histories illustrate some of the types of gastric and colonic disturbance which may be encountered and my reasons for regarding them as allergic.

CASE 7.—A medical man, aged 59, developed indigestion at a time of great strain. A suspicion of duodenal ulcer was entertained but not confirmed. At the same time he developed angio-neurotic oedema affecting the lips and eyelids particularly, and developing usually on waking in the morning. When he went on holiday he lost both the dyspepsia and the angio-neurotic oedema. Later, with an access of work and worry, the symptoms recurred and the scrotum and penis also became affected by the oedema. At this time he did not lose the symptoms on a holiday. *His father had hay-fever. Two sisters and two brothers had asthma. One sister had chronic urticaria. His daughter was asthmatic.* His dyspeptic symptoms developed between 2 and 3 hours after food, and he sometimes had hunger-pain in the night. He was sleeping badly and was very tired when I saw him.

I found no signs of organic disease, and prescribed a third partner, medinal at bedtime, and an early retirement from practice.

He wrote to me 8 months later as follows: 'You will be interested to hear that since I have had better nights my digestive apparatus has been quite a different thing, and I have had no signs of the giant urticaria which troubled me last winter.' Now, 2 years later, he has retired from practice and remains perfectly well.

Non-specific treatment, as with asthma, may sometimes play a useful part in 'unconditioning' allergic symptoms.

CASE 8. A young woman, aged 32, was brought to me by Dr. C. Boyson on account of a series of attacks of abdominal pain in the course of the descending colon, lasting perhaps 20 minutes. Six weeks and 2 years previously she had had bad attacks of pain in which she was 'doubled up'. For over ten years she had been worried by indefinite abdominal pains, and both the gall-bladder and the appendix had come under suspicion. At times she had feelings of extreme emptiness. She was of nervous type. She believed that influenza could precipitate an abdominal attack, and that worries and smoking aggravated. The gall-bladder was radiologically normal. There was indefinite tenderness in the right iliac fossa. In childhood and later she had been troubled with *eczema*, and throughout adult life by *hay-fever* and a spasmodic rhinorrhoea which was induced by proximity to horses. One brother was *asthmatic* and her father was a '*sneezer*'. Later she was seen in an attack of cholecystitis with slight icterus and local tenderness over the gall-bladder.

CASE 9. A retired mining engineer, aged 70 (referred by Dr. D. R. Pike), had suffered from heartburn for many years with aggravation latterly. He was chiefly troubled between 3 and 6 a.m., when he was wakened by oesophageal burning and spasm, choking and hiccups, and would expectorate much watery fluid. A diagnosis of duodenal ulcer had been made by one physician, although there was no radiological confirmation. He was intolerant of salt meat and Vermouth, and knew his evening cigar 'did him no good'. His mother and maternal uncles had *asthma*. He himself showed a well-marked factitious *urticaria*.

CASE 10. A married woman, aged 37, a patient of Dr. F. G. France, gave a long history of abdominal pain, had seen many physicians, and been fully investigated in a London hospital, without result or benefit. Seven years previously she had had a hysterectomy for menorrhagia and dysmenorrhoea. Her complaint was of a dull, aching, linear pain in the course of the descending colon, with aggravation by worry, exertion, and after defaecation, features characteristic of the 'spastic colon'. The stools were rather loose, and she had a feeling that the bowel was never empty. Apart from a myotonic left pupil there was no evidence of organic disease. She also suffered from *urticaria* and *hay-fever*, and her mother had suffered from *urticaria*.

CASE 11. A married woman, aged 38, with three young children, *was brought to see me, by Dr. H. W. Todd, for recurring abdominal* crises characterized by severe abdominal pain, profuse vomiting, even water being rejected, a temperature not exceeding 99°, and a quick pulse. There was general tenderness in the attacks with 'semi-rigidity', but no distension. Appendicitis had been queried. In one attack the pain was chiefly epigastric; in another right-sided. Morphine had been given on one occasion. The attacks passed over in 2

or 3 days. After her last pregnancy, a year previously, the bowels had been slightly loose. One attack had followed shell-fish. She had also had slight attacks of *angio-neurotic oedema* affecting the lip and, following the last abdominal seizure, some 'large raised bumps' on the back of the neck. She had always been liable to 'acidity' and skin troubles. In her most recent attack there was headache. On several occasions she had experienced extremely severe attacks of *rectal spasm* lasting 20 minutes. Her first baby suffered from *universal eczema*. Apart from slight deep tenderness in the right iliac fossa there was no evidence of disease.

One of the chief difficulties in cases of this type is the differentiation from appendicitis. It is also to be remembered that appendicular infection or a gall-bladder infection may (as I have more than once been led to believe) act as the 'sensitizer' in a patient with allergic tendencies. Diagnostic finality in cases of this kind may only be attained by a 'follow up' over a period of years. The association of cutaneous or other allergic phenomena with abdominal attacks can never of itself exclude a more organic basis for such attacks.

CASE 12. A married woman, aged 59, highly strung and fond of good living (seen with Dr. C. H. Atkinson), had shown unusually severe reactions to the extraction of teeth and also to vaccines prepared from them as a treatment for rheumatism. Over a period of 2 or 3 years she had several extremely severe abdominal attacks, starting with a girdle-like pain of colicky character, which at times 'doubled her up' and necessitated morphine. With some of them she experienced headache. A year prior to my being called to see her she had been troubled by a very obstinate *urticaria*, which eventually departed after calcium injections. On 12 April 1934 she felt 'off colour', nervy and irritable, and then had one of these attacks with passage of pale stools, a temperature of 101·4, and a pulse-rate of 100. This attack, like the others, passed off 'in a day or two'. Possible precipitating causes had been shell-fish, smoked salmon, and cream. She was intolerant of eggs and chocolate. As a child she had had bronchial troubles. Her doctor had seen her with spasmodic pain in the *descending colon*. *I saw her on 13 April and could find no signs* of organic disease, and was of the opinion that her pains were colonic and, perhaps, an expression of allergy. On 5 June 1934 she had a very bad attack of upper abdominal pain without vomiting; temperature 99°. There was some tenderness in the right iliac fossa. She was operated on that night for appendicitis (retro-caecal) with localized peritonitis. After her wound had healed she experienced further trouble with obscure temperatures and abdominal pains.

Summary

Cases of 'spontaneous' sensitization or allergy have been compared with cases of 'experimental' sensitization or anaphylaxis. There is a close parallelism between the symptomatologies, subjective and objective, of serum-anaphylaxis and certain rare and alarming seizures occurring without apparent cause. These seizures are characterized by simultaneous gastro-intestinal and circulatory symptoms, together with cutaneous manifestations or an associated history of these. They affect persons with individual and familial liabilities to asthma, hay-fever, and urticaria. In other persons showing similar liabilities we also discover a tendency to chronic or recurring disorders of stomach and bowel.

Generalized abdominal pain, vomiting, and diarrhoea, on the one hand, and pallor, tachycardia, and other shock-like manifestations on the other, are the features of the more severe and acute disorder. In one case I have seen severe recurrent bleeding from the bowel akin to that described by Dean and Webb in experimental anaphylaxis in dogs.[1] Recurring pain, of less intense type, in the gullet, stomach, and bowel, sometimes simulating organic disease, and looseness of the bowels are the main features of the more chronic dyspepsias.

There is little to distinguish the circulatory phenomena and subjective sensations of some vasovagal attacks (Gowers's syndrome) from those of anaphylactic shock, and cases of Gowers's syndrome may create, at the time of the attack, an equivalent degree of alarm. A case of Gowers's syndrome following a second inoculation of tetanus antitoxin is described.

Referring to my notes of nineteen cases filed under the heading of angio-neurotic oedema, I find, in addition to Case 7, two examples of associated dyspeptic disturbance and two of associated vasovagal attacks. A similar inquiry by cross-reference into my much larger asthmatic series

[1] Dean, H. R., and Webb, R. A., *Journ. of Path. and Bact.*, 1924, xxvii. 51.

would necessitate a more laborious inquiry, but the association of asthma with digestive and other allergic disorders is well recognized. With relapsing and evanescent disturbances such as those under review we depend, of necessity, for advances in our knowledge more upon detailed clinical observations and case histories than upon any other method of approach. The therapeutics of the individual case are also better served by close clinical scrutiny and adjustments based thereon than by allegiance to a particular method.

Conclusions

No abdominal or circulatory disturbance should be labelled as 'allergic' unless two or preferably more of the following postulates are fulfilled:

(1) The symptoms should bear close comparison with those observed in human anaphylaxis or serum-sickness.

(2) There should be a history of idiosyncrasy in respect of some food, beverage, tobacco, drug, or other extraneous substance.

(3) There should be observed, either in conjunction or alternating with the abdominal or circulatory episodes, other accepted allergic phenomena such as asthma, hay-fever, urticaria, or angio-neurotic oedema.

(4) There should be a family history of these disorders.

(5) The disturbances should show some such intermittency or periodicity as obtains with other allergic disorders.

(6) Every care should have been taken to exclude organic disease.

To these A. F. Hurst[1] would add the occurrence of eosinophilia and a favourable response to the therapeutic administration of adrenalin during attacks. My cases have all been seen in the course of consultative work, and I have had few opportunities of putting these additional tests to the proof.

[1] In Price's *Text-book of the Practice of Medicine*, London, 1933.

XXXIV

DIATHESIS, OR VARIATION AND DISEASE IN MAN

In the year 1884 Jonathan Hutchinson published a series of six lectures on 'Temperament, Idiosyncrasy and Diathesis', suitably entitling his book *The Pedigree of Disease* and dedicating it to the memory of Charles Darwin. His opening lecture includes the following sentences:

> 'Our forefathers, who knew far less about the details of pathology than we do, attached far more importance to such matters as temperament and diathesis. They were accustomed to prescribe for a man's temperament; we think only of his disease, and turn aside with weariness from classifications of diathesis in which the physicians of an older day delighted. Although to a large extent this change of sentiment has been the result of advance in knowledge, yet I think it might easily be shown that it has gone too far, and that we now neglect unwisely the study of those differences between man and man of which, for the most part, physiology takes no cognizance, but which may yet prove of much importance in modifying the processes of disease.'

Ten years ago these words could have been rewritten with equal truth, for the whole subject of constitution as a factor in morbidity had continued to suffer a curious neglect at the hands of our profession. This neglect was in part due to the birth and growth of bacteriology, with its concentration on the extraneous causes of disease, and in part also to the perfection of biochemical and histological methods and a preoccupation with the intimate processes and effects of disease which these in turn engendered. It is true that physicians have never omitted to place a certain reliance upon family histories, and that the genetics of a few rare maladies have been carefully and profitably studied. Until recently, however, there was little direct inquiry into the problems of constitutional predisposition and immunity. Indeed the whole doctrine of diatheses was by some subjected to a measure of ridicule which a closer attention to the teachings of Darwin and his disciples might at any time have discountenanced.

In the last few years Draper in the United States, and in this country Garrod, Hurst, Rolleston, Langdon Brown, and the writer of the present paper have endeavoured to revive interest in the study of 'those differences between man and man' which are associated with, or concerned in maintaining a liability to or freedom from, some common forms of disease. Medicine owes much to genetics and genetics owe not a little to medicine. In the future we shall look to a closer co-operation between geneticists on the one hand and students of human physiology and pathology on the other. From the physiologists in particular may we not expect a better attention to the problems of individual physiology and a clearer recognition of the fact that for no particular structure or function is it possible to establish an absolute standard of normality? Although the variations about the mean may be slight indeed they are sometimes of the greatest importance in that they serve to shape the destiny of the individual, for better or for worse, in his conflicts with natural adversity.

Morbid characters are transmissible from one generation to another in accordance with the same laws as those affecting the transmission of favourable or neutral characters. They may be conveniently subdivided into: (1) morbid structures, (2) morbid functions, and (3) morbid dispositions. Between these the differences are, perhaps, more apparent than real, for inherited morbid functions, such as colour-blindness and haemophilia, probably depend upon minute differences of cellular or molecular structure, and a morbid disposition or diathesis may be said to represent a liability to unusual or variable function or reaction in the presence of environmental stress.

Hare-lip, supernumerary digits, and achondroplasia are examples of heritable structural defect. Colour-blindness and haemophilia have already been cited as examples of inherited physiological flaw. All of these are present at birth, and, unless they be surgically corrigible, persist through life. Morbid dispositions include those peculiarities of tissue or tissue-response which carry with them in a subject healthy at birth and sometimes throughout life

n low immunity to the tubercle bacillus or other bacteria, or a liability, especially in adult life and in the presence of certain habitual or environmental influences, to such chronic or relapsing diseases as gout, asthma, migraine, epilepsy, hyperpiesia, duodenal ulcer, and pernicious anaemia. Here we are only concerned with the morbid dispositions or diatheses. Before discussing these in closer detail certain definitions of terms reclaimed for proper usage are desirable.

Constitution and Diathesis

By the term *constitution* should be understood the sum-total of inborn qualities, anatomical, physiological, psychological, and immunological, of which the individual is compounded, or his whole endowment from the parental germ-plasm. By a *constitutional disease* we should therefore imply not a general as opposed to a local disease, but one dependent upon peculiarities of constitution or the qualities of the germ-plasm.

Diathesis is described in *Dorland's Medical Dictionary* as 'a natural or congenital predisposition to a special disease'. Hutchinson [1] defined diathesis as 'any condition of prolonged peculiarity of health giving proclivity to definite forms of disease'. In naming a particular diathesis we should couple the term with the disease to which the predisposition exists, such as the 'gouty diathesis', and not with the constitutional peculiarities which are found in association with it. Hurst [2], in describing the physical characteristics encountered in association with duodenal ulcer, has used the term 'hypersthenic gastric diathesis'. It would be more correct to speak of the 'ulcer diathesis' and to state that it occurs in company with, or as a part of, the 'hypersthenic constitution'.

To maintain conformity with biological concepts I have suggested that a diathesis should be considered as 'a variation in the structure or function of tissues which renders them peculiarly liable to react in a certain way to certain extrinsic stimuli'. Sir Archibald Garrod [3] has been kind enough to give this definition his blessing in his recent monograph on inborn factors in disease.

Variation

We owe to Darwin the important conception of variation, for he showed that although, in the main, like begets like, there is also a constant tendency among species to vary in a greater or less degree and that under conditions of domesticity variability in animals is greatly increased. Naturalists have studied extensively the variability of wild forms, but this is generally slight as compared with the variability occurring, for instance, among dogs and domestic pigeons. There is, as Huxley [4] indicated, no real difficulty about the fact of variability inasmuch as the organism propagated proceeds from two stocks with different qualities and prepotencies and 'cannot be an exact diagonal of the two'. The human race also shows wide variations, and in a nation or even in a single family we still find very perceptible and distinctive variations in respect of colour, stature, temperament, stamina, ability, and longevity. These are in large part germinal, and in common with all true variations are transmissible from one generation to another. Is it surprising that we should find comparable variations in respect of liability or resistance to disease?

If a diathesis be regarded as a biological variation and, like all true variations, transmissible, it at once becomes comparable with such favourable variations as pave the way to longevity, athleticism, and high intellectual attainment. Further, it is only reasonable to argue the existence of unfavourable as well as of neutral or favourable variations. It could scarcely be otherwise. Above and below the mean or average and most convenient stature there must be, within certain limits, every conceivable variation of stature. And above or below the mean or average resistance to tuberculosis, or power to metabolize or excrete uric acid, there must, within limits, be every conceivable quantitative variation. At the extremes we meet with peculiar resistance or susceptibility to the disease in question. The case for diathesis may be put more tersely by saying that the more abnormal a man is within the limits of health and in respect of certain qualities, the more readily will he, in appropriate

circumstances, he precipitated into a particular state of ill health.

It must be clearly appreciated that *constitution* and *diathesis* are not interchangeable terms. Rather is the diathesis a part or a feature of the constitution. Physicians through the ages have recognized an association between certain diseases and certain types of physique or temperament or certain peculiarities of texture or colouring. These traits are also a part or feature of the constitution. Their presence may help to the recognition of a diathesis, but for the most part they do not explain it. Thus dark-haired, dark-complexioned people are more liable to constipation and abdominal disorders, and blue or grey-eyed subjects to the skin disease, psoriasis, but the dark hair and the blue eyes do not in any way explain these proclivities.

For a disease to be classified as constitutional, I would suggest that one or more of the following postulates are necessary: (1) a clear family history of the disease should be frequently obtained; (2) there should be frequently associated with it notable physical, physiological, or psychological peculiarities (i.e. correlated variations); (3) some peculiarity of structure or function present in health and capable of explaining the predisposition should be demonstrable.

I have elsewhere [5] discussed some of the arguments in favour of a constitutional factor in diseases as diverse as tuberculosis, rheumatic fever, scarlet fever, diphtheria, duodenal ulcer, 'visceroptosis', hyperpiesia, angina pectoris, gout, asthma, migraine, epilepsy, and pernicious anaemia. *In relation to some diseases we recognize at present only* the fact of greater or less immunity or predisposition in certain families or races. In relation to others we recognize a definite tendency for the predisposition to be passed on immediately through the generations. In relation to others, again, we may add the occurrence of correlated variations in the shape of peculiarities of colouring, physique, or temperament. Finally in a few we can go farther still and put a finger on the actual anatomical or physiological variant which seems to explain, at least in part, the particular predisposition.

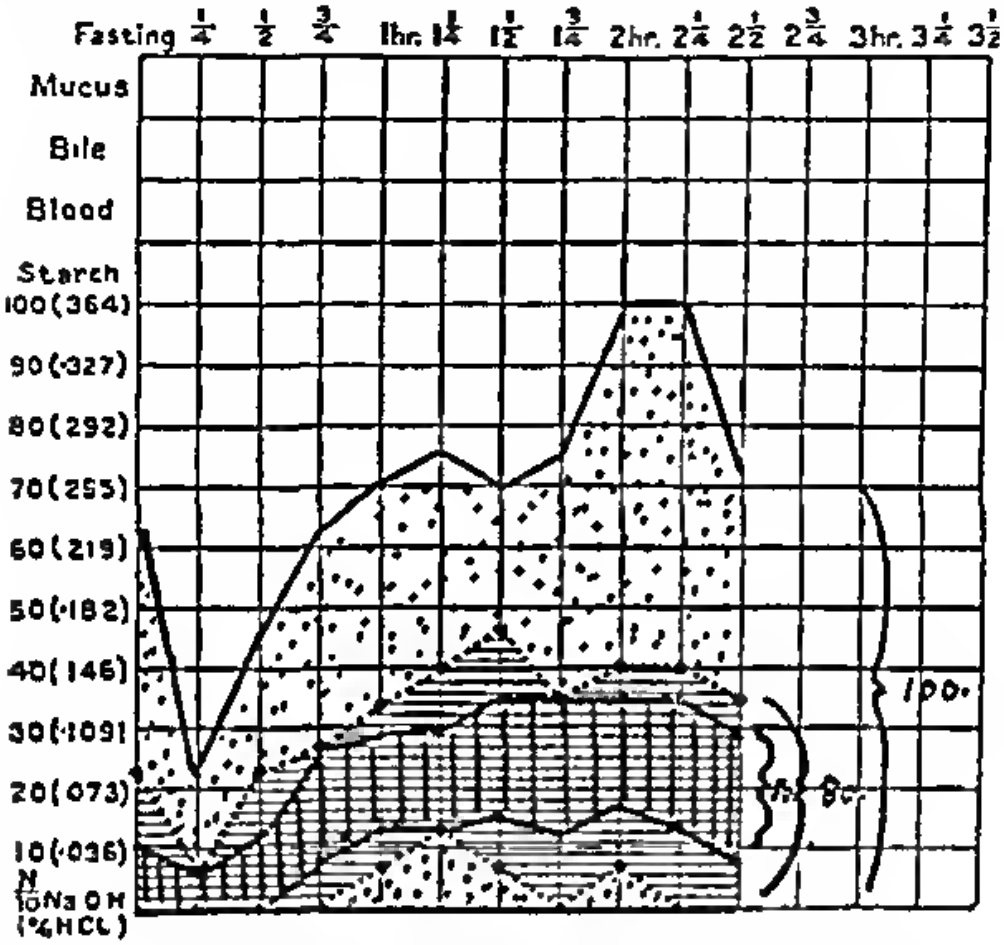
I propose to confine myself to two diseases, already reviewed in some of these connexions by Hurst [2], in which we may, employing our three postulates, recognize simultaneously the occurrence of positive family histories, of correlated variations, and of a peculiarity of function, discoverable both in patients and in the course of an investigation of healthy subjects, which appears to provide a reasonable, if partial, explanation of the actual proclivity.

The Ulcer Diathesis

In 1921 Izod Bennett [6] and I performed fractional gastric analyses on one hundred healthy male medical students. The extremes of variability in their curves of gastric acidity are shown in the accompanying chart. Eighty per cent. of the total were found to give curves falling within the limits indicated by the transverse hatching, and this zone has been adopted as the 'normal' standard for test-meal charts in clinical use. Eight healthy subjects gave curves of acidity which, on previous experience, would have been regarded as pathologically high, and of these five were of the 'climbing' hyperchlorhydric type which we now associate with duodenal ulcer.

Now the hyperchlorhydria of duodenal ulcer is not only present in the great majority of cases (70–80 per cent.), but is also constant in the individual and persists at all times whether the ulcer be active or quiescent. Experimentally in animals ulcers are perpetuated by an artificial hyperchlorhydria (Bolton). The suggestion that hyperchlorhydria, occurring as an inborn variation, is a predisposing factor to the birth, or at any rate to the perpetuation, of a duodenal ulcer becomes therefore a very reasonable hypothesis. But let us inquire into the other evidence for a constitutional factor in duodenal ulcer. First, in respect of family history, we obtain in at least 10 per cent. of all cases an account of one or more proved cases of duodenal ulcer in near relatives [7]. In one case of mine the father of the patient, two uncles, and a cousin; in another three brothers; in a third a sister and two maternal cousins had been afflicted. In a fourth family both parents, three sons, one

daughter, her son and daughter, and a paternal cousin in the middle generation had peptic ulcers; in all but two of these, and in all the males, the diagnosis was duodenal ulcer. If due allowance be made for the infrequent recognition of duodenal ulcer as a cause of dyspepsia in the last and



Variations in Gastric Acidity in Health.

preceding generations, the frequency with which the diagnosis is missed at the present day, and the numerous difficulties experienced in collecting and recording medical pedigrees, it seems probable that the true incidence of positive family histories would be appreciably higher than 10 per cent.

In respect of correlated variations we find again and again that the victim of duodenal ulcer conforms to a distinct physical and psychological type, in which a lean, muscular, energetic, and often robust habit of body accompanies a propensity for restless and conscientious activity

or a worrying disposition. Radiologically the stomach is commonly of the short, 'steer-horn' type, active and quickly emptying. Even if it be admitted, as it must be, that external influences, including occupational stress, over-smoking, the colder seasons of the year, and infection, are essential additional or determining factors, it would yet seem just to claim that a native hyperchlorhydria, in concert with the other physical and psychological variants described, furnishes just such a deflexion from the mean of healthy function as would be calculated to predispose to this disease.

The Pernicious Anaemia Diathesis

In the series of healthy students referred to above there were four whose stomachs were found to be devoid of all secretion of hydrochloric acid. Hurst [2] has argued that a considerable proportion of all cases of pernicious anaemia are consequent upon an inborn or constitutional achylia. Achylia gastrica is almost constant in this disease and is now generally accepted as an essential aetiological factor. Pernicious anaemia may also complicate the artificial achlyia of gastrectomy. In support of his view Hurst adduces: (1) the occurrence of achylia in a small proportion of healthy individuals; (2) the more frequent occurrence of achylia in the families of patients with pernicious anaemia; and (3) some striking examples in which pernicious anaemia has appeared in two or more members or generations of one family. There are, furthermore, certain correlated variations which lend colour to the constitutional hypothesis in the case of pernicious anaemia. Addison [8] noted that it occurred 'chiefly in persons of a somewhat large and bulky frame, and with a strongly marked tendency to the formation of fat'. Draper [9], with anthropometric studies, demonstrates a type of chest, generally deep, wide, and short, which he claims as peculiar to victims of the disease.

Thus in two very diverse conditions, duodenal ulcer and pernicious anaemia, we find support for the idea of constitutional predisposition (*a*) in the family history, (*b*) in the association of certain correlated variations (which proclaim

a 'type' but do not in themselves explain the predisposition), and (*c*) in the occurrence of remarkable biochemical variations which (in the light of recent research) go a long way towards explaining the liability. If it were possible to chart in a similar manner the degrees of variability in respect of other functions of the body it is probable that we should discover divergencies comparable to those shown in the case of gastric acidity, and that at the two extremes we should find an increased and diminished liability to certain types of injury or disease.

Is it not probable that the metabolism of purine bodies, if it could be measured and charted in the same graphic way, would be found in a long series of young and healthy individuals to show wide variations, and among the extremes might we not anticipate a pronounced liability to, or immunity from, gout in later life? Some day it may even become possible to 'measure' the susceptibility of the young to tuberculosis just as we can in some degree already, with the Schick and Dick tests, reveal a great or little liability to diphtheria or scarlet fever. In this event it is scarcely to be doubted that, together with familial liability or freedom and in association with distinctive physical types, we should find a parallel positiveness or negativeness in our tests.

Idiosyncrasies to foodstuffs and drugs, whatever their intimate physiological basis may be, are in the same category as diatheses. Indeed Hutchinson described idiosyncrasy, as Rolleston [10] has lately reminded us, as 'diathesis brought to a point'.

Whatever part external stresses may play, variations in psychological equipment undoubtedly do much to determine the degree of liability to the common neuroses and psychoses.

The study of constitution and diathesis is one of abounding interest and real practical value. We must needs observe the temperament, peculiarities, and individual reactions of our patients and of their near relatives with a constant watchfulness if we are to preserve a just balance in the departments of diagnosis, prognosis, and treatment. In

assessing, in respect of any disease but especially of the more chronic forms, the aetiological contribution of sex, season, occupation, environment, and infection, we can never afford to neglect the abiding contribution of original hereditary endowment. There are better inspirations to thoughtful medicine to be found in the *Origin of Species* than in a modern text-book of bacteriology. To physiology, let me repeat, we are surely entitled to look for future help in the shape of organized research into the whole problem of human variability. Few problems offer better prospects for a fruitful partnership between physiology and clinical medicine. The proper study of mankind, in sickness and in health, is always man.

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XXXV

OPENING REMARKS AT A DISCUSSION ON RESEARCH IN CLINICAL MEDICINE[1]

We may presume that the main motive for the present debate on research in clinical medicine is a prevailing sense of dissatisfaction with the achievements of clinical inquiry or with the conditions upon which achievement has to depend. I believe it no exaggeration to say that we are all at this moment alive to the existence of disturbing and retrograde tendencies in modern medicine. In the department of diagnosis, early specialization and the advent of numerous physical and chemical methods, which at first promised—and in some degree have proved competent—to enhance the science and accuracy of clinical study, have brought disappointment in their train, have hampered the natural evolution of common observation and common sense, and fostered faulty methods and an uncritical attitude in experiment. In the department of therapeutics, although there have been some notable discoveries, the same uncritical attitude and commercial enterprise have between them encouraged an empiricism quite unworthy of our age. In the department of prognosis there has not only been no general advance, but an actual loss of competence through neglect of the study of what may be called the natural history of disease in man. The time has come for a reawakening of interest in medical philosophy. Clinical practice will receive a strong stimulus to improvement when the methods of clinical science are better determined. It is part of the function of philosophy to direct or determine method.

Apart from a general and largely silent discontent there have also been two important pronouncements of late which I cannot but hold responsible in some part for the inauguration of this discussion. I refer to papers by Sir Thomas Lewis on 'Research in Medicine, Its Position and Its Needs' (*Brit. Med. Journ.*, 15 March 1930), and by Mr.

[1] *Proc. of the Royal Soc. of Med.*, 1930, xxiv. 151.

Wilfred Trotter on 'Observation and Experiment and their Use in the Medical Sciences' (*Brit. Med. Journ.*, 26 July 1930). I am sure that many, like myself, must have drawn inspiration from these papers and that there is much to be found in them on which to base the general scheme of our discussion. More recently, and since my own thoughts were put to paper, Lord Moynihan has handled the same topic in his address at the Banting Research Institute.

My first duty as opener is to indicate the boundaries of the subject, and to suggest what aspects of it we may most profitably consider. I would suggest that we might consider in turn the meaning, the methods, and the scope of modern clinical research and the opportunities which are at present, or should ideally be, provided for its proper conduct.

The Meaning of Clinical Research

Of the department of progressive medicine whose needs he is voicing, Sir Thomas Lewis writes:

> 'It may be termed *clinical science*. This science seeks, by observation and otherwise, to define diseases as these occur in man; it attempts to understand these diseases and their many manifestations, and here especially makes frequent use of the experimental method. It makes definite experiments upon disease or watches the effects of experiment conducted by injuries, however these arise; it culls, or actually creates, and uses physiological and pathological knowledge immediately related and applicable to the diseases studied. Its value has been abundantly and frequently displayed in this country by such experimental clinicians as Ferrier, Horsley, Mackenzie, and Head. The very mention of these names is in effect a definition of the science that is in mind. Their work was not work that could be delegated to laboratories; it was inspired and sustained by direct contacts with disease; it was carried through in very large or chief measure by observations on sick people.'

In defining the meaning of clinical research we cannot, I think, do better than follow this lead. Research in clinical medicine is not pathological, bacteriological, or biochemical research. These are concerned with the study of the agents, the processes and the consequences of disease in man under the conditions of the laboratory, and often with the help of experiments in animals. Clinical science should rather be

considered as a branch of the science of human biology. It studies the behaviourism of disease in man, or perhaps it would be more correct to say of man in disease. It observes, records, and, when possible, measures the processes of disease as they occur in the living subject, and within certain limitations it may control, modify, or reproduce these processes for purposes of detailed study.

The Methods of Clinical Research

The methods of all scientific research, in their broadest subdivision, are either observational or experimental. Some sciences, such as zoology and geology, are essentially observational. Others, such as physics and physiology, have depended for their progress almost entirely upon experiment. The great scientists like Harvey and Darwin have wherever possible employed both methods, calling one in support of the other. While it was a particular instruction of Harvey's that we should 'search and study out the secrets of Nature by way of experiment', in all his work and elsewhere in discussing method he couples observation with experiment, knowing them both to be indispensable in the biological sciences and complementary to one another. The great clinical scientists have all realized this, but with the growth of the ancillary sciences of physiology and pathology the natural tendency has been in the direction of a division of labour, the demands of experiment claiming certain faculties and an expenditure of time which left little opportunity for observational study, and the busy life of the physician (the student of φύσις or nature, as his name implies) allowing small scope for experiment. Scientifically it has been the misfortune, not the fault, of the physician that he has always had to expend a disproportionately large part of his energies in the treatment and management of patients. As *Lewis insists, the pursuit of curative medicine necessarily* conflicts at many points with the advancement of scientific medicine. Nevertheless many of the greatest contributions to medicine—or shall we call it physic, the science of the physician or naturalist?—have been due to members of the observational school who were practitioners of medicine.

Hippocrates, Sydenham, Bright, Laennec, and Addison were among the foremost exponents of this school and, although he cites them as examples of the experimental clinician, I am sure Lewis would admit that Maekenzie and Head owed at least as much of their achievement to the method of observation.

Both Lewis and Trotter in the papers referred to would seem to imply that the great and spacious days of observational medicine are almost numbered and thnt the future is all for experiment. Here I eannot find myself in full agreement with them. With improvements in our methods of training and observation, I believe it should be possible to add to our knowledge of man in disease eontributions as important as any of tbose made in the past and often equivalent in practical advantage to those supplied by experiment. Further, whereas the fields open to the observational physician—difficult though they be to eneompass—are many nnd varied, the scope of experiment must, by the dictates of humanity, remain somewhat strictly limited.

At this point, perhaps, we should demand a elear ruling ns to where observation ends and experiment begins. The use of instruments of precision, for instance, eannot be held to turn observation into experiment. The stethoseope, the sphygmomanometer, the electrocardiograph bave all improved our observational capaeity, but to study a patient or a series of patients with their aid eonstitutes not an experiment but n refinement of the observational method. The same may be said of radiology and the innumerable biochemical tests which have for their purpose the measurement of vital phenomena and their comparison with normal standards. If, on the other hand, we study the effects of n new drug on the action of a disordered heart with the aid of the electrocardiograph; if we strive to reproduce a gastric pain artificially and simultaneously observe the movemeats of the stomach on the fluorescent screen; if we watch the capillary responses to applications of heat or eold or the injeetion of a drug; if we invent and test a new operation; then we are employing the experimental method. In the one ease we are observing the easunl experiments of Nature;

in the other we are actually promoting small-scale experiments of our own.

When we come to a consideration of the projects and the more intimate proceedures open to the observational physician and to a comparison of these with those at present available for the experimentalist, I think we must agree that the former still has the broader programme before him. Just as in animal biology the modern trend is in the direction of studying behaviour, oecology, and genetics in the open, as opposed to laboratory inquiry, so, in my belief, the next trend in clinical medicine (or the biology of man in disease) will be in the direction of a study, at once broader and more intimate, of behaviour, personality, idiosyncrasy, vital reactions, and genetic factors in our living patients, while experimental inquiry (always, I trust, co-operative), in the hands of an expert few, runs a parallel course. Until new instruments of precision come to trial, or some new departure in pharmacology or surgery is signalled, the methods of human experiment at our disposal are, it seems to me, conspicuously few.

The Scope of Clinical Research

The contributions of the older physicians were chiefly in respect of the broader natural history of disease. By careful study of symptoms and signs, and at a later date by correlation of the phenomena observed in life with the changes found in the cadaver, they established a classification of diseases and some reasonable interpretations of symptoms. They also paid much attention, though of a superficial kind, to the influence of temperament, heredity, and environment. They often wielded well the tool of inductive reason. In their tasks they were chiefly hampered by their limited knowledge of normal physiology and by their lack of precise methods of observation. Later generations have recovered the ground they trod, adding and improving here and there by new and more accurate observations, or by the interpretation of old observations on the basis of fresh physiological and pathological knowledge. New diseases continue even now to be discovered and described by the observational

method. Important syndromes, such as those proclaiming a coronary thrombosis or a sub-arachnoid haemorrhage, have only lately been established and analysed. A more minute analysis of morbid phenomena continues to make our appreciation of the natural history of the old diseases more intimate. Where laboratory research has had an application this has generally been promptly utilized. Where laboratory research has led astray or has endeavoured to simplify when simplification was impossible, the clinical observer has often supplied the corrective. I would maintain that his task is not nearly ended.

Certain special fields for clinical research at once commend themselves. The wide realm of subjective symptomatology, which constitutes a major part of morbid physiology —and, let it be remembered, symptoms are the earliest phenomena of disease—is still largely unexplored, if we except certain important contributions to the study of pain. We ought by now to have more accurate information in our possession about nausea, heartburn, the dyspnoeas, and the many varieties of aches in body, head, and limb. It should be possible to determine with greater precision the nature of those abdominal pains which nowadays lead so constantly to fruitless surgical intervention. Symptoms as expressing particular disturbances of function and not as listed characteristics of a particular disease are clamouring for organized research. The influence of constitution on the incidence and course of the chronic diseases is just beginning to attract fresh interest, which should go far to provide a stimulus for future research, and not exclusively along the anthropometric lines laid down by Draper. In aetiological studies, socio-medical surveys of populations determined by age, sex, occupation, geography, or otherwise, and requiring the collaboration of physician, social worker, and statistician, should have not a little to teach us (*vide* Chapter XXXVI). In therapeutics there is much waiting to be done, but almost more to be undone. It should not have been necessary to wait a quarter of a century to discover by slow and bitter experience that the greater part of vaccine-therapy, as prescribed or practised by

specialists having little or no acquaintance with the natural history of disease in man, was a delusion unworthy of a scientific profession. With combined experiment and observation in accredited hospitals by trained workers it should be possible to decide within a comparatively short time what is good and what bad in the serum treatments and chemotherapies at present advocated in acute bacterial disease, and what is potent and what useless among the endocrine preparations. The principles of prognosis in acute bacterial infections and other anxious maladies should by careful observation become more surely established. Neurology has in recent times been greatly and rapidly advanced mainly by observation, but partly also by surgical experiment. In the realm of morbid psychology, which owes much of its rapid growth to the observational method, there is ample scope for further research, and by this means many diseases and disorders at present in receipt of vague physical labels will eventually find their true category.

I have mentioned but a few departments of medicine awaiting the broom of careful observational research. In several instances experiment should lend a helping hand. In each instance it seems reasonable to hope that research will bring practical advantage. But clinical research need not necessarily be utilitarian. There are many diseases of obscure causation which are worth studying for their own sake as natural phenomena. Much research in modern physiology is devoid of immediate application, and for those who have no humanitarian interest in medicine and can devote their lives to such work clinical science can also provide a wealth of problems. Among the rarer diseases and peculiarities there are some which provide for the experimentalist material especially suited to his needs.

The Opportunities for Clinical Research

We come lastly to the question of opportunity. There can be no disputing the truth of Sir Thomas Lewis's contention that at present there is no adequate provision and no adequate encouragement for the young man who would devote his life, or part of it, to clinical research. The step-

ping-stones whereby he must cross the stream between qualification and economic independence in medicine are customarily house-appointments, junior staff appointments, and, for a shorter or longer period of lean years, an assistant physicianship at a teaching hospital. Alternatively he makes general practice or specialism his goal. If he embark during any part of his probationary period upon a useful piece of research he is seldom if ever in a position to give it his full time or to find free access to the appropriate material. As a rule he does not see enough patients. As soon as practice—which is the necessary aim—begins to arrive his outlook alters, his time is consumed, and his hopes of scientifically productive work diminish. A research grant may help him here and there, but no one and no institution offers him security. Physiology and pathology, none too well endowed themselves, offer better economic opportunity than clinical science.

It is doubtful, however, whether 'curative' medicine and 'progressive' medicine, as Lewis calls them, can ever be divorced as he would wish. No one can conduct research on patients who are not under his own care, and no one can have patients under his care for research purposes and not treat them. It should, however, be possible for a promising man to be relieved of the absolute necessity of private practice and much crippling routine for a term of years, and, in special cases, through his working life. The professorial units with their assistantships do not quite fulfil the requirements. Special hospitals or wards for selected men and devoted to research purposes would defeat their own ends through creating a wrong environment, a new kind of ultra-specialism, and a separation from the healthy criticism of men engaged in teaching and practice.

In the scheme for research physicians as forecast by Sir Thomas Lewis and initiated by the Medical Research Council there are many points for criticism, but there is the germ of a good idea. To become a physician at all (whether we use the term in its oldest and best sense as meaning a student of nature, or in its modern interpretation as a healer of the sick) requires many years of initiation in a school far harder

than the schools of physiology and pathology, involving constant contact with large numbers of patients. Only from such experience can fruitful ideas and a proper balance be derived; there is no short cut. Yet Lewis requires that his men should be young and that they should be relieved, from the beginning, of the gruelling apprenticeship of out-patient work and ward-teaching and forbidden that intimate school of private practice wherein most of us find our opportunities of seeing disease in its earlier stages and more active phases, of examining intelligent patients under favourable conditions of privacy and in their natural environment, and so of gathering, in my firm conviction, our richest crumbs of instruction and inspiration. Personally I should like to see a vacancy declared from time to time at the teaching hospitals for an additional assistant physician, the appointment to be an open one and filled only if a man of outstanding merit is forthcoming. The post should supply a general medical out-patient day, a few beds, and access to all material in the hospital of use to his self-instruction and research; with certain definite restrictions in respect of time and fees, and (except in the case of acute disease) within the precincts of the hospital, he should be allowed to see private patients referred to him by colleagues familiar with his interests and his needs; the appointment should be for five years in the first instance and then either renewable indefinitely or convertible, perhaps, to an honorary assistant physicianship of the usual type; the salary should be commensurate at least with those accorded to men of junior professorial rank and, in the event of continuance of the appointment on a whole-time basis, should rise to equal those accorded to full professors. Such a research physician, although probably chiefly concerned with one or two types of disease, must have access to all types, must work in an atmo*sphere of disease considered from all points of view, and* must be in contact with senior, contemporary, and junior colleagues willing and eager to help or criticize. Whatever previous training he may have had in physiological or other laboratory method he should have held, as an introduction to the problems of man in disease, house-appointments for

a year or two at least, and for a period of not less than two or three years, a medical registrarship or tutorship, or have served a like period at special institutional medicine or in practice. In the selection of candidates credit should be given for a broad earlier education and particularly for some grounding in philosophy, logic, or psychology as against purely technical abilities or an uninterrupted scientific education from the school period. Qualities as physician or naturalist should be allowed at least as strong a claim as qualifications for research in other spheres. A scholarly heredity should, by Galtonian doctrine, be considered a very distinct advantage.

Lewis has also reviewed the possibilities of Clinical Science as a University subject, and there is much to be said in favour of his advocacy.

These matters deserve our serious consideration, and the more so because the Medical Research Council are fully alive to the importance of clinical research and are lending it the help of their endowments. The problems which it is their desire to solve are our daily problems. It is natural that we should wish to see them wisely approached.

XXXVI

THE SOCIAL PATHOLOGY OF RHEUMATIC FEVER[1]

ALL diseases of high incidence may be said to have a 'social' as well as an 'individual' pathology. Where the application of knowledge to the practical purposes of prevention—as distinct from diagnosis and treatment—is concerned, social pathology is clearly more important than human pathology in its more usual and restricted sense. The two sciences should be more closely integrated. The researches of the social pathologist are related to *ultimate* causes, and more particularly to those environmental, domestic, occupational, economic, habitual, and nutritional factors without which the *intimate* (or specific) causal factors cannot find their opportunity. They are concerned with the trends of mortality and morbidity in the community as a whole and its component groups, and with the particular influence upon these of differing social conditions. The methods of social pathology include: (i) the social post-mortem examination conducted by means of statistical analyses of official mortality figures, and correlations of these with measurable social influences; (ii) morbidity studies with similar correlations; (iii) planned *ad hoc* socio-medical surveys; and (iv) social experiments. By such methods not only the extent and trends and the consequences of community diseases, but also their aetiology can be studied as profitably as their specific aetiology and intimate morbid processes are studied in the ward, the dead-house, and the laboratory.

From mortality studies we know that the standardized *death-rate for pulmonary tuberculosis rises steeply in* passing from the higher to the lower socio-economic groups and that it is approximately twice as high in Social Class V as in Social Class I (Registrar-General's classification). The

[1] Based on an address given at the annual meeting of the Royal Sanitary Institute (*Journ. of the Royal Sanitary Inst.* 1946, lxvi. 277).

same is true for infant mortality, which at the census period 1930–2, was four and a half times higher in Social Class V than in Social Class I, the intervening classes showing intermediate figures. Valvular heart disease, the syphilitic diseases, gastric ulcer—all show the same discrimination against the lower income groups, whose environmental, nutritional, educational, and other advantages still remain grossly inferior to those of the professional and more privileged groups. Even cancer—where the upper alimentary tract and the skin are concerned—discriminates against working-class populations. Tuberculosis mortality, although continuing to fall, remains closely correlated with living conditions and accommodation and with certain occupations, and it reacts adversely to war conditions and any decline in nutritional standards. Certain occupations carry with them an all-causes mortality grossly in excess of the anticipated mortality for the male population as a whole, while others give a better expectation of life. Some lethal diseases discriminate against the higher income groups and against certain professions; among these coronary artery disease is a notable example. The social pathology of all these and many other common diseases is clearly as worthy of study and development as are those branches of human pathology which concern themselves rather with the causes, manifestations, course, and end-results of disease as it affects the individual.

Numerous papers have appeared in recent years bearing upon the social pathology of rheumatic fever, which remains, during the earlier decades of life in these islands and in many other countries, one of the most lethal and crippling of our prevailing community diseases. A review of the present state of our knowledge would seem timely, particularly having regard for impending social changes and the large rehousing programmes with which we are confronted. I have confined myself in the main to the experience of this country.

Definitions

We may include under the general title of rheumatic fever the acute and so-called sub-acute rheumatisms of

childhood, adolescence, and early adult life; juvenile chorea; and rheumatic carditis occurring with or without definitive articular manifestations, rheumatic nodules or chorea. We must accept that diagnosis is not always easy, and that, without the development of a cardiac lesion, certain transitory fevers and pains cannot with full assurance be included in our category.

Within the orbit of social pathology, we can properly consider studies bearing upon mortality, morbidity, and all those influences of environment and socio-economic status to which locality, housing, crowding, poverty, and nutritional and educational defects make, or may make, their contribution. Since the family is the smallest social unit, the influence of familial predisposition may also be included. Although they play their part in aetiology, age and sex might be regarded as individual rather than social factors, and yet both of them circumscribe a social group within the general population. Geography, climate, and season are general extrinsic influences which must be considered in all full aetiological inquiries. They are not social factors, but they may impose different degrees of stress upon different nations or social groupings.

The Size of the Problem

When we come to review the incidence of rheumatic fever and its sequels in this country, we at once find ourselves at a disadvantage for lack of morbidity figures. Mortality cannot exactly reflect morbidity, and yet our present judgements must be largely based upon mortality records. Mortality studies in the case of a disease with an initial onset usually preceding death by many years cannot inform us accurately about the distribution or secular trend or the possible social and environmental associations of the disease at its inception.

It has been estimated (Morris and Titmuss) [1] that there are nearly 200,000 cases of rheumatic heart disease at all ages in this country. Parkinson [2] suggests a present figure of at least 200,000 cases of heart disease in Great

Britain, mostly rheumatic, between nges 18 nnd 41, and (citing Stocks) that the annual deaths in England and Wales from rheumatic heart disease may be considered as in the neighbourhood of 16,000. Close upon 100 per cent. of deaths from heart disease before the age of 40 are a consequence of rheumatic carditis, which is second only as a cause of death to pulmonary tubereulosis in females between 5 and 45, and follows tuberculosis and violence in males. Before the war it accounted for 2 per cent. of nll deaths in England and Wales and 10 per cent. of the deaths between 5 and 45 [3].

Estimates from hospital sources of the proportion of rheumatic children developing heart disense have varied between 50 per cent. and 90 per cent. As hospitals are concerned with the more serious cases, and minor and 'subclinical' infections (as in the case of pulmonary tuberculosis) are probably common and must often pass unrecorded or unrecognized, reliable estimates nre not at present possible. Bach *et al.* [3] report that in 1038 the London County Council card index of children up to 15 who were suffering from or had suffered from rheumatic infections, included 22,800 children, or about 2·6 per cent. of the child population. Pre-war estimates of the incidence of rheumatic heart disease in school children have varied between 1 per cent. and 5 per cent. In London it was estimated that the incidence of rheumatic heart disease in school children had fallen from 2 per cent. to 0·77 per cent. between 1926 and 1937 [3]. The incidence of the disease and the deaths in the early acute phase of rheumatic fever in children are both declining. Hospital physicians of mature experience would probably agree that serious initial attacks with polyarthritis, pericarditis, and hyperpyrexia have become more rare in their lifetime, but valvular disease continues to complicate many of the less severe rheumatic episodes. Special hospitals, clinics, schools, and other provisions are inadequate for the needs of all the damaged hearts. The direct and indirect costs of the disease to the community must be very heavy. Socially and nationally, the problem remains a large and serious one.

Specific Factors

Brief reference must be made to the intimate or specific factors, as distinct from the ultimate factors, in aetiology.

Although agreement has yet to be finally reached on the subject, evidence steadily accumulates in favour of *Streptococcus pyogenes* (or certain of its serological types) as the infective agent. Sore throats, or other infections of the upper respiratory tract, commonly precede the individual rheumatic attack; epidemics of streptococcal sore throat in partially closed communities have frequently been accompanied or followed by epidemics of rheumatic fever with carditis in a proportion of the population at risk. Hospitalized cases of rheumatic heart disease too commonly develop streptococcal infections with secondary attacks of carditis in the course of ward epidemics of sore throat. Serological reactions in rheumatic children support the theory of an initiating streptococcal infection. There is also some evidence that, while the sulphonamide drugs have no good effect on the rheumatic attack, their prophylactic use may so far protect against streptococcal infections of the upper respiratory tract as to reduce significantly the incidence of rheumatic recurrences in treated, as contrasted with control, groups. Barclay and King-Lewis [4], summarizing the American trials, quote these as recording 1·2 per cent. of rheumatic relapses in 501 patient seasons (treated series), as compared with 19·8 per cent. of relapses in 505 patient seasons (untreated series). Experiences in this country have been less encouraging.

There is also, however, strong evidence for considering the rheumatic attack as a specific type of response occurring at a susceptible age in the case of individuals having an inborn or acquired sensitivity to a common agent—an agent which, in most persons, provokes a local reaction only, or produces other types of general response. The rheumatic attack, like other sensitization phenomena, follows the throat infection, not immediately, but after an interval which may extend to two or more weeks. Its articular and cutaneous phenomena, like those of serum

sickness, are transitory. The occurrence of rheumatic families, with the disease appearing in successive generations and among individuals in those generations living in differing environments, and sometimes even under favourable social conditions [5], and also the fact that the majority of children living under unfavourable conditions do not acquire the disease, would favour the hypothesis that—as in many other types of infection and acquired illness—there are, at the two ends of the scale, types which are genetically more or less susceptible to infection, or more or less liable to develop a sensitized state in the presence of infection.

Bearing on the genetic factor, Read *et al.* [6] investigating the siblings, parents, uncles and aunts, and grandparents of rheumatic and control children, found a significantly higher incidence in each relationship among the former than among the latter. Pickles [5] reported an interesting family in which, among 53 descendants of a man—himself a victim of rheumatic heart disease—23 had suffered from rheumatic fever, or had unmistakable signs of mitral stenosis. Most of them were prosperous, well housed, and well fed. Specific liability, as well as specific infection, must be accorded fair consideration.

Season, Climate, and Geography

Primary and subsequent attacks of rheumatic fever are especially common in this country in the period October to March—the period in which the respiratory tract infections have their highest incidence. It has been stated that the disease is more common in northern than in hot southern climates, but the medical statistics of tropical countries are at present unsatisfactory and the rarity of rheumatic fever in countries such as India should not be over-emphasized. In Madras, in 1944, I was shown a number of cases of grave rheumatic heart disease in a single ward of one hospital. The squalor and poverty in many of the working-class districts of Indian cities are appalling and, although seasonal and weather variations may be less favourable there than in our own country to the occurrence and spread

of catarrhal infections, density of population and living conditions should he far more so. Young [7] concluded from mortality studies, which revealed a correlation between the deaths from rheumatic fever and from heart disease in the regions covered, that there was a higher incidence of rheumatic heart disease in the western counties than elsewhere in England and Wales.

Social Factors

Physicians have long recognized that rheumatic fever and heart disease are relatively rare in private practice among the well-to-do, as compared with their experience of hospital practice and working-class populations. This impression is supported hy statistical investigations of mortality and hy special surveys. Young [8]; Miller [9]; the Medical Research Council's report on 'Social Conditions and Acute Rheumatism' [10]; Bruce Perry and Fraser Roberts [11]; Poynton [12]; Holland Clarke [13]; and, more recently, Morris and Titmuss [1]; Daniel [14]; and Donovan [15]; have all adduced or discussed evidence which shows that rheumatic heart disease has a strong correlation with poverty, or, rather, with the complex of adverse circumstances which accompany poverty. Morris and Titmuss [1] show that mortality increases on the whole with density of population, and that depressed rural districts return rates as high as the worst of the hig towns; they also associate a *subsequent* rise in the mortality from rheumatic heart disease (hetween ages of 5 and 25) in the English and Welsh county boroughs with the economie slump of 1930–2 [16]. London, Manehester, Liverpool, Bristol, aad Glasgow have heen particularly mentioned as homes of the disease. Bruce Perry and Fraser Roberts [11] found a significant association between the density of persons per room in Bristol and the incidence of rheumatic heart disease. Daniel [14], also in Bristol, revealed a significant association with differeaces in family income and significant variations with the numher of rooms used by each family divided by the numher of persons in the family. Miller [9] concluded tbat there was a higher incidence in the artisan class than in the poorest

group, but this view is not supported by Morris and Titmuss [1]. Of the factors operating within the general framework of poverty, damp houses have often been suspect, and Daniel found slight suggestive evidence of the effect of living or sleeping in basements. Crowding, with increased liability to droplet infections, would seem to be more definitely incriminated.

Nutritional deficiency, with impaired resistance to infection, has naturally been suggested as a factor dependent upon low economic status. Warner and Winterton [17] discovered no appreciable signs of under-nourishment in rheumatic children as compared with a control group, but considered that animal protein and the dairy product components of the dietary in the social groups studied were lower than they should be. Coburn and Moore [18] were more strongly inclined to incriminate sub-standard diets, but not a deficiency of any one dietary factor. Holland Clarke [13], describing his Dublin experience, was more impressed in all working-class occupational grades by the factor of bad housing and sleeping accommodation than by that of low family budgets. Green [19], on the other hand, in an epidemic of rheumatic fever among naval apprentices, found a much higher incidence among the less-favoured Tyneside boys than among boys from other parts of the country who were similarly exposed.

Before the other influences associated with poverty are too strongly incriminated, the effects of crowding *without* poverty or nutritional deficiency should be considered. If droplet infection with the streptococcus is, as is now widely accepted, an important specific factor, local epidemics might be expected to occur among boys or girls or young adults well cared for in other respects but subjected to *overcrowding through defective dormitory spacing. Such* local epidemics have occurred in training ships and in barracks, where other influences, whether in respect of nutrition or open-air exercise and recreation, were not unfavourable. Dudley [20] gave an account of the high incidence of sore throats and rheumatic attacks in training ships and establishments, but was inclined to blame damp

and chill more than crowding. Green [19] described similar outbreaks among naval apprentices living at close quarters and partly in huts, although muddy approaches and wet feet may here have been a factar. Glover [21] found that the incidence af acute rheumatism among army recruits in barracks was directly correlated with aver-crowding. Feasby [22] has discussed rheumatic fever in relation to streptococcal infections in the Canadian Army during the war, and Hare [23], accepting the association, has reviewed methods af preventian of streptococcal epidemics and rheumatic fever in the armed forces. In the U.S.A., streptococcal and rheumatic fever outbreaks among naval and military personnel have also presented a considerable problem during the war. Crowding in barracks or huts of boys or men still at a suseeptible age would seem—as in the case of cerebrospinal meningitis [21]—to be the likely common factor in the various outbreaks described. If damp and chill are potent factors, why was rheumatic fever so rare in young soldiers during the trench warfare of 1014–18?

Although rheumatic fever has had a low incidence in British public schools, Bradley [24] reported two outbreaks of streptococcal sore throat at a well-to-do public school housing 340 boys. There were twenty-nine attacks of acute rheumatism, affecting 25 boys, and among these 20 cases of carditis. He stated that hygienic arrangements were satisfactory, 'except for some overcrowding and the fact that the boys live in one building and not in separate houses'. Here such factors as damp or chill and present or antecedent dietary shortage could be reasonably excluded.

Social studies af individual cases af rheumatic fever in children—and here the hospital ar municipal almoner as medical social worker has an important part to play—will frequently reveal the adverse conditions in which a child has been living before the first ar subsequent attacks. Home visits can also pravide other important evidence bearing upon the varied role of a common infective agent in a domestic epidemic [25]. The damestic epidemic of streptococcal infection is, indeed, warthy of much closer

study. In two cases of rheumatic carditis in children which I employed recently as texts for a socio-medical student conference, the family budgets were considered adequate, but the bedroom accommodation was inadequate. In 1937 I saw the following case with W. H. Bradley, the account of which he included later in a paper on the spread of streptococcal disease [25]:

'On March 2, 1937, Gwendoline, daughter of a farm labourer in an English village, went to bed with a bad cold, and felt ill until March 6. On March 7, however, she got up because her mother was delivered of a baby—the eighth in the family. She helped nurse her mother, who, on March 10, became suddenly ill with puerperal fever, associated with a scarlatiniform rash, from which she eventually died. Fourteen days after the onset of the mother's illness, the father had "influenza", and Evelyn, aged 4, contracted a severe cold 2 days later, while 5 days later, on April 1, Gladys, aged 17, had a cold, and on April 7, Fred, aged 14, contracted "influenza". On April 6, Gwendoline was troubled with pains in her lower abdomen, which persisted for 3 days. She was vaguely unwell until April 9, when her illness declared itself as typical rheumatic fever. Type 15/17 streptococci were recovered from the throats of 4 of these patients, but were absent from the mother's throat. A pure culture of this organism was, however, obtained from the pus in a pelvic abscess subsequently operated upon.'

Without this specific domestic investigation the child and her mother might have been admitted to the same hospital and clinically and pathologically investigated there in the usual manner without any connexion being established between the two cases, and without any light being thrown upon those adverse social influences in the absence of which both of them might have remained well. The family, as the smallest social unit, is as worthy of investigation as are the larger types of population. It can also be more intimately and humanely studied, and with reference to psychological and genetic as well as to economic and other influences.

The Extension of Social Inquiry

While the conditions of life of the working-class population may to-day be accepted as a main aetiological factor in rheumatic fever and carditis, it is—as has been

suggested—not enough to blame poverty without considering the influences within the framework of poverty which are particularly responsible. Here we must confess that we are badly in need of fuller information bearing upon urban, rural, institutional, and domestic epidemiology. Morbidity must supplement mortality studies. How can the information be collected? Many writers have advocated notification, and it has been locally operated. I confess that its general enforcement now seems to me to have become an urgent necessity. Parkinson's [2] recent insistence that 'compulsory notification of rheumatic fever is essential to any effort to deal with it on a national scale' will probably be widely endorsed. Without it, we can learn little more of the secular trend of the disease or of regional or seasonal fluctuations. Without it, local health officers are not in a position to conduct planned surveys; to inquire into the domestic and other conditions obtaining in individual cases; to consider under the effects of crowding the respective contributions of restricted space, damp, poor ventilation and lighting and, possibly, blanket-dust; or to pursue over a period of years the results of such experiments of opportunity as are made possible at a time of rehousing. How far will the trend of rheumatic fever in a city with a high incidence be influenced by the gradual transfer of ill-housed populations to new estates? How far are secondary attack-rates in individuals affected by improved sleeping accommodation and better-built houses? To what extent may day-school, as distinct from domestic, epidemics of sore throat have an effect on the rheumatic fever rate? Should the institutional epidemic be related to heightened bacterial virulence, or, more simply, to heightened atmospheric concentration of bacteria with increased exposure risks—in fact, to bacterial as well as human 'crowding'? *Here are some questions awaiting answer.*

In discussing social pathology, it would be outside my province to consider how important to the individual case immediate investigations of home conditions on notification, earlier removal to hospital, and subsequent domiciliary visits on discharge from hospital, might be. It is, however,

reasonable to suggest that organized domestic studies might make important contributions to the better understanding of the natural history of the disease both in individuals and in the community, and thereby, in due course, to prevention and treatment.

Notification

There is no sound reason why notification should be reserved for the more obviously communicable diseases. If it can be shown to be in the general interests of the public health and can, sooner or later, assist the prevention of a common, costly, and crippling disease, it is obviously sound policy, whether from the point of view of hygiene, humanity, or economics. We must not, however, overlook certain difficulties which might be connected with notification. The more obvious difficulties and how they might be met are briefly considered hereunder:

1. The diagnosis of rheumatic fever is often much more difficult than that of any of the common exanthemata, but perhaps not greatly more so than that of pulmonary tuberculosis in its early stages. As in the case of the last-named disease, consultant and other facilities are likely, in the near future, to become available in all cases of doubt.

2. Unlike the common exanthemata, rheumatic fever is often recurrent. Should secondary attacks be reported? What should be the criteria for notifying primary and secondary attacks? Should a rheumatic heart lesion discovered for the first time in a child or adolescent in the absence of recent activation be notified? It might be stipulated that for purposes of central registration, all cases of juvenile rheumatism and chorea, and of acute carditis and valvular disease in young persons, believed to be of rheumatic origin and seen for the first time, should be notified locally and centrally; while all secondary attacks should be locally notified in order to ensure the fullest possible co-operation between practitioner, local health authority and consultant, and the full use of special clinics or social services. Old-established rheumatic heart disease, not recently reactivated, and seen for late cardiac symptoms

or discovered in the course of a general examination, should not be notified.

Summary

If social medicine, in its broadest connotation, is to be given its fullest practical opportunity, it must be scientifically supported by a sound pathology. The social pathology of a disease is largely dependent upon reliable clinical, statistical, and social data, and especially upon morbidity and mortality figures and their correlations with measurable social influences.

In tuberculosis, while we are all agreed that mortality studies alone are not enough, we have been slow to make full use of our material bearing upon morbidity. Benefiting by our experience and omissions in respect of tuberculosis, it should be possible to utilize notifications of rheumatic fever and carditis more effectively from the moment of their introduction, and thereby more expeditiously to advance our understanding of causes and prevention. In support of statistical analyses of official returns, planned socio-medical surveys in large cities, intimate domestic studies, and long-term social experiments in populations destined for rehousing, should also have a part to play. The disease has been very closely studied in the individual—living and dead. It should now be our aim to maintain a continuing study of the living disease in the community, and in the process—valuable though they must remain—to rely less exclusively upon the methods of the social post-mortem examination.

Conclusions

Poor social circumstance, and especially the conditions accompanying working-class life in large cities, have been established in this country and elsewhere as having outstanding aetiological importance in rheumatic fever.

Of the factors operating within the general framework of poverty, overcrowding is probably the most potent. The fact that outbreaks of streptococcal sore throat and rheumatic fever occur in residential schools, training ships,

and barracks, where general hygiene, nutrition, and medical supervision are usually good, supports this view. Crowding itself, however, is a further subject for study, for limitation of cubic space is not the sole factor at work. Defective ventilation and lighting, and dust, may all help to maintain too high a concentration of noxious bacteria. Disturbed sleep and lack of opportunity for open-air play may impair resistance to infection.

Actions prompted by general aetiological considerations should not be postponed until specific aetiologies are clarified.

Compulsory notification of rheumatic fever would greatly assist those epidemiological and aetiological studies upon which the further development of preventive action must be based.

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XXXVII

THE HIPPOCRATIC IDEAL[1]

THE sources of inspiration in medicine and the medical sciences are many and varied. There are advantages at all times, but especially in an age of swift material progress, stern competition, and perplexing prospects, in pausing occasionally to consider the motives which prompt us and the beliefs which sustain us in our choice of career and in our daily work. As a profession closely concerned with the health and affairs of the individual and the community we are exposed not a little to criticisms both of a private and a public kind, and, partly at the direction of the modern press, which thrives on scandal and open dissection of human frailties, we have come, perhaps, to incur a larger measure of censure than was allotted to earlier generations of doctors. Whether the criticisms we encounter have relation to our manners and peculiarities, our education, our attitude to unorthodox therapy, our jealousies, our technical failures, or to other defects in our constitutions and our actions, and unjust though many of them may be, we would be foolish and conceited to suppose that none of them are ever well grounded. We are human and fallible. Our problems both of science and of practice are far too difficult for us to adopt an attitude of complacency or superiority.

Science forges ahead, often to the embarrassment of practice; times and habits change and ethics suffer. At the present time there are, I would submit, many cogent reasons for a review of motives and beliefs and for a discussion of those ideals without which no body of scientists or humanists can profitably proceed. The beginning of a new session, the meeting of an old and honoured society commemorative in name and aims of the work of a great man, and the precincts of one of the oldest and finest

[1] An address delivered to the Abernethian Society, St. Bartholomew's Hospital, 15 November 1934 (*Lancet*, 1934, ii. 1263).

hospitals and medical schools in the world, provide an appropriate occasion and place for such a review.

I have said that the sources of inspiration in medicine are many and varied. Uncritically, perhaps, for our life is full and exacting and we have small time for personal analysis, we all of us perceive that our steps have been directed and our endeavours supported on the one hand by the humane and on the other by the scientific interests of medical work, and, even through times of tedium or disappointment, and while recognizing that our labour is also our livelihood, most of us continue to be actuated by these interests.

The inspiration of our teachers and the traditions of our school, of contemporary discoveries such as those of Banting and of Minot, of the journals and the monographs, and, by no means least, of the *medical society*—upon the moral and practical value of which Osler was so rightly insistent—all these lend their quota. Too few of us are tempted to explore the attractive field of medical history, and yet not one of us goes forth into the world without some consciousness of his debt to those old masters who are more to the eras of medicine than kings and governments have been to the eras of social and political history. The experiment of your own immortal Harvey; the clinical method of Sydenham; the work of the physician-pathologists Bright, Addison, Hodgkin, and Wilks in my own school; Jenner's discovery; the contributions of Pasteur and Lister; and the brilliant advances due to the physiologists in the last century, have provided us with a wealth of inspiration upon which each of us must continue to draw through life in greater or less degree.

But it is my purpose to go back to a far earlier period for a source of inspiration which, through many centuries, was accounted the most profound and inexhaustible of all, and to show you that, with all our multitudinous discoveries and fresh forms of knowledge, we can still find in the work and wisdom of Hippocrates, and of those who composed the Hippocratic school, a method, a science, an art of practice, and a code of professional conduct upon which, as supplying a foundation and an ideal, no subsequent generation has

been able to improve. I shall hope to persuade you that occasional readings of Hippocrates are by no means out of date or a waste of time; to stir in those of you who do not already possess it a veneration for one of the noblest figures in that rich and lovely age of Grecian culture; and to remind you that, lacking all the benefits of physiology and pathology, Hippocrates has nevertheless left us lessons in clinical method and record, observations on prognosis, a rational therapeutic system, and, in addition, an outline of medical ethics, from which we can derive instruction and correction to this day.

In case you should doubt the reasonableness of an appeal to such ancient doctrine I need but remind you that philosophers in all subsequent ages have found the chief fountain of their inspiration in the writings of men who were the near contemporaries of Hippocrates, and that just as the Socratic Dialogues of Plato have remained an essential introduction for the student of philosophy and the Bible an essential introduction for the student of Christian morals, so might the Hippocratic Collection, or at least selected readings therefrom, serve as an introduction for the student of the medical arts and sciences. It is a pity that the practical demands of medical education and the incessant developments and discoveries of the clinical and ancillary sciences should, by degrees, but so largely, have excluded the desire for contact with early authority. It is our loss, too, that no individual to-day is so equipped intellectually as to be able again to stand aside and take the general view of medicine in its entirety, to correlate its problems, to balance its science with its art, to perceive and assess the components which make up the intricate 'whole' presented to us in the shape of a 'disease' or a 'sick man'. We have become, inevitably, *too knowledgeable* and *too specialized*. In the endeavour to think sufficiently anatomically or physiologically; sufficiently in terms of infection and the immunity-response; to assess the constitutional, the environmental, and the psychological factors in the individual case—or, in other words, to bring together our too disjointed knowledge for the solution of the individual puzzle—we commonly

fail or achieve but a partial success, and in our treatment we often interfere too much. Sometimes, I believe, Hippocrates, with all his limitations, would have succeeded where we fail through his simple habit of observing and noting the facts of nature, through having seen the same things before, through his recognition of disease as a natural process rather than an 'abnormality' (which after all is but a small advance on the old idea of demonic possession), and through his clear recognition of the *vis medicatrix naturae*. But I move ahead of my theme.

Life and Work of Hippocrates

Of the details of the life of Hippocrates little is known, but we have evidence that he flourished in the fifth century B.C., that his period of greatest activity was in the latter half of that century, and that he lived to a great age.

His contemporaries included the statesman Pericles; the poets Aeschylus, Sophocles, and Euripides; Socrates and Plato, the philosophers; Herodotus and Thucydides, the historians; and Phidias, the sculptor. He came of physicianly stock, and probably received a part of his early training in the temples of Health from his own father. The school which he founded was in the little island of Cos in the Aegean Sea. In the market-place of the chief town of Cos there still stands a very aged plane tree which is reputed to have flourished in his day, and in the shade of which he is believed to have taught. Expert opinion has pronounced it possible for the tree to have endured such longevity. In his later years Hippocrates travelled much. His advice was in great demand, and he won in his lifetime a degree of respect and veneration foreshadowing and in full keeping with his later fame.

The Hippocratic Collection consists of a number of writings on medical and allied topics, some of which are ascribed directly to Hippocrates himself, some (which may yet be regarded as genuine products of his school) to his disciples, and others which are now accounted as spurious and of later date. Among the more noteworthy of these

writings are the following: *Epidemics*, I and III; *Airs, Waters, Places*; *The Aphorisms*; *Prognostic*; *Regimen in Health*; *Regimen in Acute Disease*; *The Oath*; *Wounds of the Head*; *Fractures*; *Joints*; *The Sacred Disease*.

Of his work and practice we may assume that he probably saw and advised his patients and taught at a temple of Health or its equivalent, much as a modern physician might hold his clinic. Probably his case records and those of his assistants were accumulated in the library of the institution. Of the case-report system he may be regarded as the founder. We have no doubt from his vivid descriptions of fever cases in *The Epidemics* that he also visited patients in their homes. Occasionally his opinion was sought by public authorities in great emergencies, as when Athens was afflicted with plague.

The Scientific Ideal

What was the great contribution of Hippocrates to the science of medicine? The advancement of the biological sciences, of which human pathology is surely not the least, has depended upon the combined contributions of observation and experiment. The method of experiment was a late arrival and, although there were experimenters before his time, Harvey may be regarded as its first outstanding exponent. Hippocrates was literally the founder of the observational method, and in this we may claim for him an even greater regard than that implicit in his familiar title, the Father of Medicine. We have to imagine that before his day medicine was compounded in large part of first aid, quackery, and superstition, and that even physicians of repute relied far more upon tradition and speculation than upon recorded fact. Hippocrates set himself steadfastly against speculative philosophies and quack therapy, and applied himself to the task of accumulating knowledge of disease and of man in disease by accurately recording what his own senses revealed to him. The method was extended to the whole realm of natural history by Aristotle, but it is a matter for pride that a physician (and the physician's work

bears close similarities with that of the natural historian) was its founder. Prof. J. S. Haldane, in his Gifford lectures on *The Sciences and Philosophy* (1927–8), writes as follows:

'Hippocrates treated the unconscious activities of life as natural processes. He claimed the right to interpret them in accordance with actual observation, regardless of superstition and of the intrusion of philosophical opinions not based on observation of them. In observing Nature just as she appears in the phenomena of life, and basing his opinions directly on the observations, he founded scientific medicine, and with it, as it seems to me, scientific biology. The co-ordinated activity manifested in the phenomena of life was regarded by Hippocrates as nothing more than a visible and tangible manifestation of Nature. . . . His influence, through Aristotle and later Greek thinkers and observers, appears to have been a very great one. . . . It seems to me that the attitude of Hippocrates was, and is, the only attitude possible in scientific biology.'

And yet how constantly has specialization, in medicine and biology, led to a neglect of the 'co-ordinating activity' in nature. How constantly to-day are we 'side-tracked' into a contemplation of isolated functions and 'parts' and a neglect of 'wholes'. Instead of man we study the parts of man; instead of disease, aspects of disease.

Only a reading of the works themselves can convey a full idea of the remarkable powers of observation possessed by Hippocrates. All his senses, seeing, hearing, feeling, smelling, tasting, must have been assiduously employed, and his deliberations, based on his sense-data, were illuminated by the clear light of his reason. He has left us living thumb-nail sketches of many diseases, including mumps, the malarias, erysipelas (mentioning how the hair falls after erysipelas of the scalp), empyema, puerperal fever. He described a number of valuable signs both of a general and a local kind. The Hippocratic facies of impending death 'with sharp nose and hollow eyes'; Hippocratic succussion in pyo-pneumothorax; 'curved nails' or, as we should call them, 'clubbed fingers' in empyema; splenic enlargement in malaria; Cheyne-Stokes breathing, 'respirations rare and large with long intervals', to use his own words; tetanus after wounds —are all depicted in his records. With no means at his disposal for minute analysis he yet gave the most careful

attention to the naked-eye characters of the excreta and of discharges.

In *Precepts* he advises that 'one must . . . occupy oneself with facts persistently, if one is to acquire that ready and infallible habit which we call "the art of medicine". For so to do will bestow a very great advantage upon sick folk and medical practitioners. Do not hesitate to inquire of laymen, if thereby there seems likely to result any improvement in treatment.' The most scientifically trained among us are still too easily tempted to toy with hypotheses instead of occupying themselves with facts. The practitioner remains unduly reluctant to accept help or suggestions from the layman. In *Law* he states 'there are in fact two things, science and opinion; the former begets knowledge, the latter ignorance'. In our modern medicine, swayed by the intricacy of our problems, we are still sadly prone to guesses and 'opinions' which warp the truth-seeking spirit. In *Ancient Medicine* and other works we find references to the constitutional factor, and in *Airs, Waters, Places* to the environmental factors in disease.

Prognosis

Hippocrates attached a very particular importance to prognosis.

> 'I hold', he said, 'that it is an excellent thing for the physician to practise forecasting. For if he discover and declare unaided by the side of his patients the present, the past and the future, and fill in the gaps in the account given by the sick, he will be the more believed to understand the cases, so that men will confidently entrust themselves to him for treatment. Furthermore, he will carry out the treatment best if he know beforehand from the present symptoms what will take place later.'

Much unnecessary and unwise treatment, both medical and surgical, might be avoided even now if physicians and surgeons, less wedded to medicines, injections, and techniques, and less susceptible to the impulse 'to do something' in anxious situations, schooled themselves better in that knowledge of the natural course and eventualities of disease upon which all sound prognosis and treatment depend.

Hippocrates knew the importance of many prognostic signs and often enough their limitations. 'If a part of the white appear when the lids are closed, *should the cause not be diarrhoea or purging, or should the patient not be in the habit of so sleeping*, it is an unfavourable, in fact a very deadly symptom.' Plucking at the bed-clothes in fevers and pneumonia he also recognized as of grave import, and also grinding the teeth in fevers '*unless it has been a habit from childhood*'. I would ask you to note how the qualifications which I have italicized complete the accuracy of the observations. The advancement of diagnosis and prognosis has depended and will continue to depend more upon exact clinical observation than upon any other single factor.

'In cases of ulcerated tonsils', he tells us, 'the formation of a membrane like a spider's web is not a good sign', and 'ulcers on the tonsils that spread over the uvula alter the voice of those who recover'. He notices that injuries or incisions on one side of the brain produce spasms on the other side of the body. His instructions for the careful examination of head-wounds, with a note on the importance of discovering if the bone is bare and of distinguishing natural sutures from traumatic fissures, are as useful to-day as when they were written.

Aphorisms

His *Aphorisms*, many of them beautifully brief and to the point, are clearly the crystallized fruits of repeated observation and accumulated experience. Here are a few of them:

'Old men endure fasting most easily, then men of middle-age, youths very badly, and worst of all children, especially those of a liveliness greater than ordinary.'

'When sleep puts an end to delirium it is a good sign.'

'Spontaneous weariness indicates disease.'

'In every disease it is a good sign when the patient's intellect is sound and he enjoys his food. The opposite is a bad sign.'

'Those who are constitutionally very fat are more apt to die quickly than those who are thin.' (The life insurance societies know this well.)

'Pains and fevers occur when pus is forming rather than when it has been formed.'

'A convulsion supervening upon a wound is deadly.'

'Consumption occurs chiefly between the ages of eighteen and thirty-five.'

'If diarrhoea attacks a consumptive patient it is a fatal symptom.'

'Apoplexy occurs chiefly between the ages of forty and sixty.'

'In the case of a person afflicted with hiccough, sneezing coming on removes the hiccough.'

'In acute diseases chill of the extremities is a bad sign.'

'Whenever abscess of the liver is treated by cautery or the knife, if the pus flow pure and white, the patient recovers, for in such cases the pus is in a membrane; but if it flows like as it were lees of oil, the patient dies.'

Was he contemplating surgery and the early substitutes for diathermy in malignant growth when he wrote: 'Those diseases that medicines do not cure are cured by the knife. Those that the knife does not cure are cured by fire. Those that fire does not cure must be considered incurable'?

The examiners may require us to know the calcium content of the blood and the technique of the Wassermann reaction. The aphorisms are more useful in practice.

In describing his bedside method and the things particularly to be observed there Hippocrates wrote as follows:

'With regard to diseases, the circumstances from which we form a judgement of them are—by attending to the general nature of all, and the peculiar nature of each individual—to the disease, the patient and the applications—to the person who applies them, as that makes a difference for better or worse—to the whole constitution of the season, and particularly to the state of the heavens and the nature of each country; to the patient's habits, regimen and pursuits, to his conversation, manners, taciturnity, thoughts, sleep, or absence of sleep, and sometimes his dreams, what and when they occur; to his picking and scratching; to his tears; to the alvine discharges, urine, sputa and vomitings, and to the changes of diseases from one to another; to the deposits whether of a deadly or critical character; to the sweat, coldness, rigor, cough, sneezing, hiccough, respiration, eructation, flatulence, whether passed silently or with a noise; to haemorrhage and haemorrhoids; from these and their consequences we must form our judgement.'

Could we desire a more concise exhortation to attentive history-taking and clinical observation?

His philosophy with regard to disease and its origins is portrayed in the beautiful fragment entitled *The Sacred Disease*, the name given to epilepsy, a disorder considered

for centuries after Hippocrates to be an evidence of demoniac possession:

> 'I am about', he says, 'to discuss the disease called "sacred". It is not, in my opinion, any more divine or more sacred than other diseases, but has a natural cause, and its supposed divine origin is due to men's inexperience, and to their wonder at its peculiar character.' And again: 'It has the same nature as other diseases, and the cause that gives rise to individual diseases. It is also curable, no less than other illnesses, unless by long lapse of time it be so ingrained as to be more powerful than the remedies that are applied. Its origin, like that of other diseases, lies in heredity.'

In the same work he discusses the brain as the seat of consciousness and the emotions, a conception quite unfamiliar at that period, when the heart and the diaphragm were commonly held to be the seat of the soul.

Observation and Record

The importance of accurately observing and recording facts; of studying the whole event and all attendant circumstances; of viewing the phenomena of disease as natural phenomena and not as due to malign agencies or, as we should say, 'abnormalities'; these, in brief, are the main lessons of the Hippocratic creed. To-day, as then, the physician, if he would be a good healer, must first be a good natural historian. The scientific ideal in medicine does not of necessity demand intensive study of minutiae, prolonged specialistic inquiry, or training or discovery by experiment alone. Rather does it require insistence on truth, correction of error, an understanding of the methods whereby truth is ascertained, an ability to sift evidence, and an appreciation of 'wholes' and of those co-ordinating activities which determine the nature of things, and without some understanding of which our study of 'parts' may become an enfeebling or confusing rather than an enlightening process. Properly used and weighed bedside experience can point the way to the goal of biological truth as surely as the departmental experience of the laboratory.

To what extent does modern medical education help us to apply the Hippocratic method or subserve the Hippocratic ideal? In the clinical period the opportunity is there

for all, even if the material of wards and out-patients be too limited, lacking much that the life of practice provides. We have also the guidance of our teachers and the stimulus of contact with other minds pursuing the same ends, but we must confess that the constant increments to knowledge and the steady arrival of new diagnostic tests and implements encumber us with difficulties, and in some degree hamper both the use of the unaided senses and the growth of judgement. Invaluable though our accessory methods of inquiry have become, we also know that in practice many of the best diagnoses and nearly all the best decisions in emergencies are accomplished without radiological or laboratory aids. In the pre-clinical period, although a thorough grounding in chemistry, physiology, and anatomy is an obvious necessity, it seems to me that the curriculum provides little scope for the cultivation of 'the habit of observation'. In the dissecting-room we train our hands and the anatomical sense, rediscovering what has often been described, but we also exhaust our memories with names of parts, and we do not learn to see new and vital things for ourselves. In physiology, the most valuable of the ancillary subjects, we find our introduction to the experimental method, and usefully train the mind to think in terms of function, but we tend to lose the applications of such knowledge and have to accept a number of doctrines liable themselves to flux and change, and altogether have so much to absorb that we commonly cease to inquire. Much of this basic knowledge in anatomy and physiology is essential; much of the detail otherwise. We use the microscope and the test-tube, and we must know how to use them, but little is done to exercise the unaided senses, the inquisitive 'look-about-you' faculty, the sympathetic appreciation of vital phenomena as shown in human feelings and actions, or to train the mind to detect the moods and passions and psychological peculiarities of other minds. Indeed, for the first three years of the medical curriculum, the observing faculty, which is so sharp in the unencumbered child, so necessary in the naturalist and the physician, and which was developed in so remarkable a degree by Hippocrates, is not only not encouraged, but to

some extent inhibited by educational modes which seek to harbour the scientific spirit with a type of training suitable for the student of physics or chemistry, but inappropriate for the student of man in health and disease. On entering the wards we have to develop a new orientation and a new method, and in the process most of what we have garnered in the pre-clinical period, and even much of what was useful therein, rapidly goes by the board.

One of my own teachers, a great surgeon, clinician, and pathologist, the late Sir Charters Symonds, urged in his Hunterian Oration fourteen years ago that clinical opportunities should be given from the very first. 'The student of medicine', he said, 'throughout his life must be sensible of the atmosphere which surrounds the sick-bed.' And again: 'The only opportunity the student of medicine has for independent observation . . . is in the clinical field, and the sooner he is brought there the better.' Many of us share these sentiments. The ward, the out-patient clinic, the consulting-room, and the home are the only places in which we can learn the Hippocratic method at first-hand.

The Therapeutic Ideal

Among the critics of Hippocrates, and even this great man has had a few detractors, there have been those who objected that he was so intent upon observing disease that he neglected his patients. Through his influence, they would aver, other physicians in other ages have been guilty of scientific callousness. In hospital work the temptation to be interested in man's pathology rather than in man himself is one which some find difficult to resist, but that is to be traced rather to a narrow curiosity than to callousness, and it must be rare indeed for it to lead to neglect. I have found nothing in my own reading of the Hippocratic Collection to justify the criticism as directed against its author. Recognizing disease processes in the body as a contest between the body tissues and other natural agencies, and aware of the spontaneous tendency to recovery in the great majority of diseases and the great majority of patients, he concluded that recovery from disease, just like

disease itself or death from disease, was a natural phenomenon. 'Nature', he or one of his followers said, 'is the physician of diseases.' Sydenham expressed himself more strongly when he declared that 'To imagine Nature incapable to cure diseases is blasphemy; because that would be imputing imperfection to the Deity, who has made a great provision for the preservation of animal life'. With our more intimate understanding of pathology we continue to support this doctrine. We continually relieve suffering by surgery, psychotherapy, and the judicious employment of diet and drugs, but, if we except the knife in certain types of injury and local disease, a few specific chemicals in bacterial or protozoal diseases, the substitution therapies, and one or two life-saving antitoxic sera, with all of which we lend a dramatic assistance to nature, we must confess that we are to this day powerless in the strict sense to cure disease.

We have ample evidence that Hippocrates did not withhold, any more than we do, the assistance which physician and nurse may give to patients to enable them the better and the more speedily and comfortably to combat their maladies.

In surgery he insisted on cleanliness, using wine for washing wounds and urging that dryness should be secured in lacerated wounds; he instructed the surgeon to keep his nails short; he trephined for certain head injuries; he taught methods of reducing dislocations which we still employ; he recognized the therapeutic value of rest, and of hot and cold applications, and of baths, and the inadvisability of prescribing alcohol in head injuries. He was an advocate of barley water in fevers and used hydromel and oxymel, giving indications for each. He was a good psychologist, as indeed every successful physician must be. Thus he speaks of the necessity of performing actions in the sick-room 'calmly and adroitly', of giving orders 'with cheerfulness and serenity'; but sometimes of 'reproving sharply and emphatically'. He advises keeping 'a watch on the faults of the patients, which often make them lie about the taking of things prescribed'. 'One must not', he says, 'be anxious about fixing a fee. For I consider such a worry to be harmful

to a troubled patient, particularly if the disease be acute.... For, in heaven's name, who that is a brotherly physician practises with such hardness of heart as not at the beginning to conduct a preliminary examination of every illness and prescribe what will help towards a cure, to heal the patient and not to overlook the reward, to say nothing of the desire that makes a man ready to learn?'

'Loud talking', we are reminded, 'is painful. Overwork calls for gentle dissuasion. A wooded district benefits.'

He is alive to the disagreements existing among physicians in the matter of therapeutic beliefs, and of the discredit which this brings them in the minds of the laity. He makes astute observations such as the following: 'For if disease and treatment start together, the disease will not win the race.' I am reminded by this in our modern medicine of the remarkable effects of antitoxin administered early, before the spread of toxins, in diphtheria and infected wounds, as compared with the much more dubious influence of antistreptococcal and antipneumococcal sera, which can seldom be given before the disease is established and declared. 'Do not', he says 'disturb a patient either during or just after a crisis, and try no experiments, neither with purges nor with other irritants, but leave them alone.' Regimen in health and disease receive full consideration, but, realizing the variability of the constitution of man and his circumstances, he admits that 'it is impossible to treat of the regimen of man with such a nicety as to make the exercises exactly proportionate to the amount of food'. He believes in giving responsibilities to dressers and clerks, and to the patient.

'Let one of your pupils be left in charge, to carry out instructions without unpleasantness, and to administer the treatment.' 'The art has three factors: the disease, the patient and the physician. The physician is the servant of the art. The patient must co-operate with the physician in combating the disease.'

But perhaps the greatest therapeutic principle of all those which the Coan school has left to us is this: 'As to diseases, make a habit of two things—to help, or at least to do no harm.' As experience accumulates many of us must relue-

tantly confess that we see a vast deal of harm in practice due to injudicious interference. The policy of 'letting well alone' in an improving case, even though improvement be slight, is a sound one, but often ignored. The urge 'to do something' in the acute or anxious case, even though it be not clear what that 'something' should be, often prevails, when it would have been far wiser to wait and watch. Against the countless triumphs of surgery we have to set a long list of harmful interferences, especially in the abdominal field. The more potent a treatment is for good, the more potent also is it for ill when misapplied. It is important to avoid timidity in our actions or a permanent policy of *laissez-faire*, but in being bold we should never become oblivious to the wise restraint of that injunction to 'do no harm'.

The Ethical Ideal

If there be present need for a revision, in the light of early teaching, of our ideas relating to the science and art of medicine, the occasion is, perhaps, still more ripe for a revision of ethical ideas. The War, as though in some small compensation for vast evil, brought benefits to medical and surgical knowledge, but its interruptions have in some degree been damaging to the old ethical standards of the profession. The former friendly relationship between doctor and doctor and patient and doctor, although they are still among the happier rewards of practice, have been subjected to various strains, and, if there has been more freedom of thought and action, this has sometimes been counterbalanced by a loss of mutual trust and understanding.

I hear occasional complaints from older men that appropriation of patients by newcomers, criticisms of colleagues to patients and by patients, and uncorrected inconstancy among patients manifest in their flittings after specialist and unorthodox opinion, are much more common than in the old days. Cloaked advertisement, 'stunt' treatments, and commercial methods have crept in insidiously in some quarters. Jealousies are rife. These evils are not new, but if there be any truth in the impression that they are increasing it is time that a profession, which has hitherto main-

tained its standards at a very high level, should immediately seek to set its house in order.

The rules were all laid down between two and three thousand years ago in the *Oath*, the *Precepts*, the *Decorum*, *Physician*, and *Law* of the Hippocratic Collection.

In the *Oath* the physician swears among other things that:

'Whatsoever I shall see or hear in the course of my profession, as well as outside my profession in my intercourse with men, if it be what should not be published abroad, I will never divulge, holding such things to be holy secrets.'

We cannot too often remind ourselves of the importance of professional secrecy or too closely guard our tongues from gossip.

Of the physician it is written that:

'The prudent man must also be careful of certain moral considerations—not only to be silent but also of a great regularity of life, since thereby his reputation will be greatly enhanced; he must be a gentleman in character, and being this he must be grave and kind to all.'

'Physicians who meet in consultation must never quarrel, or jeer at one another. For I will assert upon oath, a physician's reasoning should never be jealous of another. To be so will be a sign of weakness. . . . You must also avoid adopting, in order to gain a patient, luxurious headgear and elaborate perfume. For excess of strangeness will win you ill-repute. . . . Yet I do not forbid you trying to please, for it is not unworthy of a physician's dignity. . . . A physician does not violate etiquette even if, being in difficulties on occasion over a patient and in the dark through inexperience, he should urge the calling in of others, in order to learn by consultation the truth about the case.'

Consideration for the patient's pocket could scarcely be more nicely prescribed than in the following words:

'I urge you not to be too unkind, but to consider carefully your patient's super-abundance or means. Sometimes give your services for nothing, calling to mind a previous benefaction or present satisfaction. And if there be an opportunity of serving one who is a stranger in financial straits, give full assistance to all such. For where there is love of man, there is also love of the art.'

Here then we have, in these few quotations, sane and kindly recommendations for the physician's life, requiring of him a high morality, devotion to professional secrecy, avoidance of jealousy, willingness to confer with colleagues,

avoidance of undue 'show', and kindness to patients in the matter of fees. We need no other code.

Disciples of the Hippocratic Method

It might seem invidious to select from the pages of medical history men who have exemplified the Hippocratic type above their fellows. In every era, although there were dark gaps in the Middle Ages, and in every civilized country there have been physicians, eminent or obscure, who have faithfully pursued the old ideal. Sydenham well earned his title of 'the English Hippocrates' in his professional life and by his endeavour to give a true description of the natural history of diseases. William Heberden, who gave the first account of angina pectoris in all its clinical details, and insisted on careful note-taking, was of similar breed. Trousseau and Osler, great teachers and practitioners, were of the same genus. But countless others among physicians and surgeons and among general practitioners of the lovable, cultured type of Dr. John Brown—the author of *Rab, and his Friends*—have fulfilled the Hippocratic behest. Among our own colleagues and teachers and family doctors we could name not a few besides. If we look beyond the anecdotes which grew around John Abernethy and have given him a reputation for uncouthness, we must agree to include him in the same school. Another great surgeon, Syme of Edinburgh, accounted Abernethy the finest surgical mind after John Hunter and Percival Pott, but he was a physician too, a physiologist, and even a psychologist, for he wrote a well-reasoned little essay on the Mind. He saw things whole, and based his views and treatment on sound observation and common sense. His generosity to poor patients is proverbial and can seldom have been surpassed.

The Future of Medicine

How shall we weld the methods of Hippocrates and Harvey to obtain the fullest benefits of both? How are we to combine the old with the new? Experimental medicine, full of gifts, firing the imagination and claiming the industry of the younger generations, but moving ahead with too

little co-ordination and control; the old steady observational medicine, no less scientific in careful hands, but often betrayed by lack of accuracy and care; and the art of practice based upon an admixture of these sciences with human kindliness and vision and courage and much restraint—how, in our individual and professional lifetime, are we to accomplish a wiser use and application of these three? How again are we to modify our curriculum and examination system in such a way as to lighten the burden of the student and yet give him firmer foundations and a broader view?

For myself I should like to appeal for better opportunities for observational training and the use of the senses in field natural history during the school period, and better opportunities for continuing the education of the senses by parallel clinical study of the healthy and the sick during the pre-clinical phases of medical education. Eyes, hands, ears, and nose, and the technique of history-taking, require constant utilization and free scope. To quote Dr. John Brown: 'In a word, let me say to my young medical friends, give more attention to steady common observation—the old Hippocratic *ἀκρίβεια*, exactness, literal accuracy, precision, niceness of sense; what Sydenham calls the natural history of disease. Symptoms are universally available: they are the voice of nature. . . .'

Human psychology, in its daily practical bearings (and more than half of practical medicine is psychology), must take its place beside a more applied and less elaborate human anatomy, physiology, and pathology. Specialism in education (and most pre-clinical and extra-clinical teachers have, of necessity, the specialist outlook) carries with it the same disadvantages as too early specialism in practice. It discourages the free use of the senses and reasoned correlation of facts, and delays the growth of judgement, which is the clinician's crowning need. If we are to breed more and better specialists it is also, to my thinking, essential that we should preserve a just balance by breeding more and better workers in the field of general medicine.

In the domain of practice, whether we come eventually

to a State service or move forward in our present paths, we must seek to temper our new science and indispensable discoveries with what our fathers possessed in better measure than we do—the old Hippocratic principles of art and conduct. In every branch we need something of the philosophy of the man who, with all his vast learning and achievement, was humble enough to realize, as his most famous aphorism reminds us, that 'Life is short, the Art long, opportunity fleeting, experience treacherous, and judgement difficult'. With the aid of such wise humility and his strong exhortations to patient research and a love both of truth and man, we shall one day combine the new with the old, resolving present difficulties, and raise the standards of the Science and Art of Medicine to a level at present beyond our vision.

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